Online Research @ Cardiff

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository: https://orca.cardiff.ac.uk/id/eprint/112749/

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Anttila, Verneri, Bulik-Sullivan, Brendan, Finucane, Hilary K., Walters, Raymond K., Bras, Jose, Duncan, Laramie, Escott-Price, Valentina ORCID: https://orcid.org/0000-0003-1784-5483, Falcone, Guido J., Gormley, Padhraig, Malik, Rainer, Patsopoulos, Nikolaos A., Ripke, Stephan, Wei, Zhi, Yu, Dongmei, Lee, Phil H., Turley, Patrick, Grenier-Boley, Benjamin, Chouraki, Vincent, Kamatani, Yoichiro, Berr, Claudine, Letenneur, Luc, Hannequin, Didier, Amouyel, Philippe, Boland, Anne, Deleuze, Jean-François, Duron, Emmanuelle, Vardarajan, Badri N., Reitz, Christiane, Goate, Alison M., Huentelman, Matthew J., Kamboh, M. Ilyas, Larson, Eric B., Rogaeva, Ekaterina, St George-Hyslop, Peter, Hakonarson, Hakon, Kukull, Walter A., Farrer, Lindsay A., Barnes, Lisa L., Beach, Thomas G., Demirci, F. Yesim, Head, Elizabeth, Hulette, Christine M., Jicha, Gregory A., Kauwe, John S.K., Kaye, Jeffrey A., Leverenz, James B., Levey, Allan I., Lieberman, Andrew P., Pankratz, Vernon S., Poon, Wayne W., Quinn, Joseph F., Saykin, Andrew J., Schneider, Lon S., Smith, Amanda G., Sonnen, Joshua A., Stern, Robert A., Van Deerlin, Vivianna M., Van Eldik, Linda J., Harold, Denise ORCID: https://orcid.org/0000-0001-5195-0143, Russo, Giancarlo, Rubinsztein, David C., Bayer, Antony ORCID: https://orcid.org/0000-0002-7514-248X, Tsolaki, Magda, Proitsi, Petra, Fox, Nick C., Hampel, Harald, Owen, Michael J. ORCID: https://orcid.org/0000-0003-4798-0862, Mead, Simon, Passmore, Peter, Morgan, Kevin, Nöthen, Markus M., Rossor, Martin, Lupton, Michelle K., Hoffmann, Per, Kornhuber, Johannes, Lawlor, Brian, McQuillin, Andrew, Al-Chalabi, Ammar, Bis, Joshua C, Ruiz, Agustin, Boada, Mercè, Seshadri, Sudha, Beiser, Alexa, Rice, Kenneth, van der Lee, Sven J., De Jager, Philip L., Geschwind, Daniel H., Riemenschneider, Matthias, Riedel-Heller, Steffi, Rotter, Jerome I, Ransmayr, Gerhard, Hyman, Bradley T., Cruchaga, Carlos, Alegret, Montserrat, Winsvold, Bendik, Palta, Priit, Farh, Kai-How, Cuenca-Leon, Ester, Furlotte, Nicholas, Kurth, Tobias, Ligthart, Lannie, Terwindt, Gisela M., Freilinger, Tobias, Ran, Caroline, Gordon, Scott D., Borck, Guntram, Adams, Hieab H.H., Lehtimäki, Terho, Wedenoja, Juho, Buring, Julie E., Schürks, Markus, Hrafnsdottir, Maria, Hottenga, Jouke-Jan, Penninx, Brenda, Artto, Ville, Kaunisto, Mari, Vepsäläinen, Salli, Martin, Nicholas G., Montgomery, Grant W., Kurki, Mitja I., Hämäläinen, Eija, Huang, Hailiang, [illegible]ng, Jie, Sandor, Cynthia ORCID: https://orcid.org/0000-0002-8905-1052, [illegible]ber, Caleb ORCID: https://orcid.org/0000-0001-8063-7674, Muller-Myhs[illegible]k, Bertram, Schreiber, Stefan, Salomaa, Veikko, Loehrer, Elizabeth,

information services
gwasanaethau gwybodaeth

Göbel, Hartmut, Macaya, Alfons, Pozo-Rosich, Patricia, Hansen, Thomas, Werge, Thomas, Kaprio, Jaakko, Metspalu, Andres, Kubisch, Christian, Ferrari, Michel D., Belin, Andrea C., van den Maagdenberg, Arn M.J.M., Zwart, John-Anker, Boomsma, Dorret, Eriksson, Nicholas, Olesen, Jes, Chasman, Daniel I., Nyholt, Dale R., Avbersek, Andreja, Baum, Larry, Berkovic, Samuel, Bradfield, Jonathan, Buono, Russell, Catarino, Claudia B., Cossette, Patrick, De Jonghe, Peter, Depondt, Chantal, Dlugos, Dennis, Ferraro, Thomas N., French, Jacqueline, Hjalgrim, Helle, Jamnadas-Khoda, Jennifer, Kälviäinen, Reetta, Kunz, Wolfram S., Lerche, Holger, Leu, Costin, Lindhout, Dick, Lo, Warren, Lowenstein, Daniel, McCormack, Mark, Møller, Rikke S., Molloy, Anne, Ng, Ping-Wing, Oliver, Karen, Privitera, Michael, Radtke, Rodney, Ruppert, Ann-Kathrin, Sander, Thomas, Schachter, Steven, Schankin, Christoph, Scheffer, Ingrid, Schoch, Susanne, Sisodiya, Sanjay M., Smith, Philip ORCID: https://orcid.org/0000-0002-3491-4519, Sperling, Michael, Striano, Pasquale, Surges, Rainer, Thomas, G. Neil, Visscher, Frank, Whelan, Christopher D., Zara, Federico, Heinzen, Erin L., Marson, Anthony, Becker, Felicitas, Stroink, Hans, Zimprich, Fritz, Gasser, Thomas, Gibbs, Raphael, Heutink, Peter, Martinez, Maria, Morris, Huw R., Sharma, Manu, Ryten, Mina, Mok, Kin Y., Pulit, Sara, Bevan, Steve, Holliday, Elizabeth, Attia, John, Battey, Thomas, Boncoraglio, Giorgio, Thijs, Vincent, Chen, Wei-Min, Mitchell, Braxton, Rothwell, Peter, Sharma, Pankaj, Sudlow, Cathie, Vicente, Astrid, Markus, Hugh, Kourkoulis, Christina, Pera, Joana, Raffeld, Miriam, Silliman, Scott, Boraska Perica, Vesna, Thornton, Laura M., Huckins, Laura M., Rayner, N. William, Lewis, Cathryn M., Gratacos, Monica, Rybakowski, Filip, Keski-Rahkonen, Anna, Raevuori, Anu, Hudson, James I., Reichborn-Kjennerud, Ted, Monteleone, Palmiero, Karwautz, Andreas, Mannik, Katrin, Baker, Jessica H., O'Toole, Julie K., Trace, Sara E., Davis, Oliver S. P., Helder, Sietske G., Ehrlich, Stefan, Herpertz-Dahlmann, Beate, Danner, Unna N., van Elburg, Annemarie A., Clementi, Maurizio, Forzan, Monica, Docampo, Elisa, Lissowska, Jolanta, Hauser, Joanna, Tortorella, Alfonso, Maj, Mario, Gonidakis, Fragiskos, Tziouvas, Konstantinos, Papezova, Hana, Yilmaz, Zeynep, Wagner, Gudrun, Cohen-Woods, Sarah, Herms, Stefan, Julià, Antonio, Rabionet, Raquel, Dick, Danielle M., Ripatti, Samuli, Andreassen, Ole A., Espeseth, Thomas, Lundervold, Astri J., Steen, Vidar M., Pinto, Dalila, Scherer, Stephen W., Aschauer, Harald, Schosser, Alexandra, Alfredsson, Lars, Padyukov, Leonid, Halmi, Katherine A., Mitchell, James, Strober, Michael, Bergen, Andrew W., Kaye, Walter, Szatkiewicz, Jin Peng, Cormand, Bru, Ramos-Quiroga, Josep Antoni, Sánchez-Mora, Cristina, Ribasés, Marta, Casas, Miguel, Hervas, Amaia, Arranz, Maria Jesús, Haavik, Jan, Zayats, Tetyana, Johansson, Stefan, Williams, Nigel ORCID: https://orcid.org/0000-0003-1177-6931, Dempfle, Astrid, Rothenberger, Aribert, Kuntsi, Jonna, Oades, Robert D., Banaschewski, Tobias, Franke, Barbara, Buitelaar, Jan K., Arias Vasquez, Alejandro, Doyle, Alysa E., Reif, Andreas, Lesch, Klaus-Peter, Freitag, Christine, Rivero, Olga, Palmason, Haukur, Romanos, Marcel, Langley, Kate ORCID: https://orcid.org/0000-0002-2033-2657, Rietschel, Marcella, Witt, Stephanie H., Dalsgaard, Soeren, Børglum, Anders D., Waldman, Irwin, Wilmot, Beth, Molly, Nikolas, Bau, Claiton H.D., Crosbie, Jennifer, Schachar, Russell, Loo, Sandra K., McGough, James J., Grevet, Eugenio H., Medland, Sarah E., Robinson, Elise, Weiss, Lauren A., Bacchelli, Elena, Bailey, Anthony, Bal, Vanessa, Battaglia, Agatino, Betancur, Catalina, Bolton, Patrick, Cantor, Rita, Celestino-Soper, Patrícia, Dawson, Geraldine, De Rubeis, Silvia, Duque, Frederico, Green, Andrew, Klauck, Sabine M., Leboyer, Marion, Levitt, Pat,

Maestrini, Elena, Mane, Shrikant, De-Luca, Daniel Moreno-, Parr, Jeremy, Regan, Regina, Reichenberg, Abraham, Sandin, Sven, Vorstman, Jacob, Wassink, Thomas, Wijsman, Ellen, Cook, Edwin, Santangelo, Susan, Delorme, Richard, Rogé, Bernadette, Magalhaes, Tiago, Arking, Dan, Schulze, Thomas G., Thompson, Robert C., Strohmaier, Jana, Matthews, Keith, Melle, Ingrid, Morris, Derek, Blackwood, Douglas, McIntosh, Andrew, Bergen, Sarah E, Schalling, Martin, Jamain, Stéphane, Maaser, Anna, Fischer, Sascha B., Reinbold, Céline S., Fullerton, Janice M., Guzman-Parra, José, Mayoral, Fermin, Schofield, Peter R., Cichon, Sven, Mühleisen, Thomas W., Degenhardt, Franziska, Schumacher, Johannes, Bauer, Michael, Mitchell, Philip B., Gershon, Elliot S., Rice, John, Potash, James B., Zandi, Peter P., Craddock, Nicholas ORCID: https://orcid.org/0000-0003-2171-0610, Ferrier, I. Nicol, Alda, Martin, Rouleau, Guy A., Turecki, Gustavo, Ophoff, Roel, Pato, Carlos, Anjorin, Adebayo, Stahl, Eli, Leber, Markus, Czerski, Piotr M., Cruceanu, Cristiana, Jones, Ian ORCID: https://orcid.org/0000-0002-1682-9134, Posthuma, Danielle, Andlauer, Till F.M., Forstner, Andreas J., Streit, Fabian, Baune, Bernhard T., Air, Tracy, Sinnamon, Grant, Wray, Naomi R., MacIntyre, Donald J., Porteous, David, Homuth, Georg, Rivera, Margarita, Grove, Jakob, Middeldorp, Christel M., Hickie, Ian, Pergadia, Michele, Mehta, Divya, Smit, Johannes H., Jansen, Rick, de Geus, Eco, Dunn, Erin, Li, Qingqin S., Nauck, Matthias, Schoevers, Robert A., Beekman, Aartjan TF, Knowles, James A., Viktorin, Alexander, Arnold, Paul, Barr, Cathy L., Bedoya-Berrio, Gabriel, Bienvenu, O. Joseph, Brentani, Helena, Burton, Christie, Camarena, Beatriz, Cappi, Carolina, Cath, Danielle, Cavallini, Maria, Cusi, Daniele, Darrow, Sabrina, Denys, Damiaan, Derks, Eske M., Dietrich, Andrea, Fernandez, Thomas, Figee, Martijn, Freimer, Nelson, Gerber, Gloria, Grados, Marco, Greenberg, Erica, Hanna, Gregory L., Hartmann, Andreas, Hirschtritt, Matthew E., Hoekstra, Pieter J., Huang, Alden, Huyser, Chaim, Illmann, Cornelia, Jenike, Michael, Kuperman, Samuel, Leventhal, Bennett, Lochner, Christine, Lyon, Gholson J., Macciardi, Fabio, Madruga-Garrido, Marcos, Malaty, Irene A., Maras, Athanasios, McGrath, Lauren, Miguel, Eurípedes C., Mir, Pablo, Nestadt, Gerald, Nicolini, Humberto, Okun, Michael S., Pakstis, Andrew, Paschou, Peristera, Piacentini, John, Pittenger, Christopher, Plessen, Kerstin, Ramensky, Vasily, Ramos, Eliana M., Reus, Victor, Richter, Margaret A., Riddle, Mark A., Robertson, Mary M., Roessner, Veit, Rosário, Maria, Samuels, Jack F., Sandor, Paul, Stein, Dan J., Tsetsos, Fotis, Van Nieuwerburgh, Filip, Weatherall, Sarah, Wendland, Jens R., Wolanczyk, Tomasz, Worbe, Yulia, Zai, Gwyneth, Goes, Fernando S., McLaughlin, Nicole, Nestadt, Paul S., Grabe, Hans-Jorgen, Depienne, Christel, Konkashbaev, Anuar, Lanzagorta, Nuria, Valencia-Duarte, Ana, Bramon, Elvira, Buccola, Nancy, Cahn, Wiepke, Cairns, Murray, Chong, Siow A., Cohen, David, Crespo-Facorro, Benedicto, Crowley, James, Davidson, Michael, DeLisi, Lynn, Dinan, Timothy, Donohoe, Gary, Drapeau, Elodie, Duan, Jubao, Haan, Lieuwe, Hougaard, David, Karachanak-Yankova, Sena, Khrunin, Andrey, Klovins, Janis, Ku?inskas, Vaidutis, Lee Chee Keong, Jimmy, Limborska, Svetlana, Loughland, Carmel, Lönnqvist, Jouko, Maher, Brion, Mattheisen, Manuel, McDonald, Colm, Murphy, Kieran C., Nenadic, Igor, van Os, Jim, Pantelis, Christos, Pato, Michele, Petryshen, Tracey, Quested, Digby, Roussos, Panos, Sanders, Alan R., Schall, Ulrich, Schwab, Sibylle G., Sim, Kang, So, Hon-Cheong, Stögmann, Elisabeth, Subramaniam, Mythily, Toncheva, Draga, Waddington, John, Walters, James ORCID: https://orcid.org/0000-0002-6980-4053, Weiser, Mark, Cheng, Wei, Cloninger, Robert, Curtis, David, Gejman, Pablo V., Henskens,

Frans, Mattingsdal, Morten, Oh, Sang-Yun, Scott, Rodney, Webb, Bradley, Breen, Gerome, Churchhouse, Claire, Bulik, Cynthia M., Daly, Mark, Dichgans, Martin, Faraone, Stephen V., Guerreiro, Rita, Holmans, Peter ORCID: https://orcid.org/0000-0003-0870-9412, Kendler, Kenneth S., Koeleman, Bobby, Mathews, Carol A., Price, Alkes, Scharf, Jeremiah, Sklar, Pamela, Williams, Julie ORCID: https://orcid.org/0000-0002-4069-0259, Wood, Nicholas W., Cotsapas, Chris, Palotie, Aarno, Smoller, Jordan W., Sullivan, Patrick, Rosand, Jonathan, Corvin, Aiden, Neale, Benjamin M. and Anney, Richard ORCID: https://orcid.org/0000-0002-6083-407X 2018. Analysis of shared heritability in common disorders of the brain. Science 360 (6395) , eaap8757. 10.1126/science.aap8757 file

Publishers page: http://dx.doi.org/10.1126/science.aap8757 <http://dx.doi.org/10.1126/science.aap8757>

Please note:
Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies. See
http://orca.cf.ac.uk/policies.html for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.

Title: Analysis of Shared Heritability in Common Disorders of the Brain

Authors:

Verneri Anttila*[1,1,2,3], Brendan Bulik-Sullivan[1,3], Hilary K. Finucane[4,5], Raymond Walters[1,2,3], Jose Bras[6,7], Laramie Duncan[1,2,3,8], Valentina Escott-Price[9], Guido Falcone[10,11,12], Padhraig Gormley[1,2,3,13], Rainer Malik[14], Nikolaos Patsopoulos[15], Stephan Ripke[1,2,3,16], Zhi Wei[17], Dongmei Yu[2,13], Phil H. Lee[2,13], Patrick Turley[1,3], Benjamin Grenier-Boley[18,19,20], Vincent Chouraki[18,19,20,21], Yoichiro Kamatani[22,23], Claudine Berr[24,25,26], Luc Letenneur[27,28], Didier Hannequin[29,30], Philippe Amouyel[18,19,20,21], Anne Boland[31], Jean-François Deleuze[31], Emmanuelle Duron[32,33], Badri N. Vardarajan[34], Christiane Reitz[35], Alison M. Goate[36], Matthew J. Huentelman[37], M. Ilyas Kamboh[38], Eric B. Larson[39,40], Ekaterina Rogaeva[41], Peter St George-Hyslop[41,42], Hakon Hakonarson[43,44,45], Walter A. Kukull[46], Lindsay A. Farrer[47], Lisa L. Barnes[48,49,50], Thomas G. Beach[51], F. Yesim Demirci[38], Elizabeth Head[52], Christine M. Hulette[53], Gregory A. Jicha[54], John S.K. Kauwe[55], Jeffrey A. Kaye[56], James B. Leverenz[57], Allan I. Levey[58], Andrew P. Lieberman[59], Vernon S. Pankratz[60], Wayne W. Poon[61], Joseph F. Quinn[62,63], Andrew J. Saykin[64], Lon S. Schneider[65], Amanda G. Smith[66], Joshua A. Sonnen[67,68], Robert A. Stern[69], Vivianna M. Van Deerlin[70], Linda J. Van Eldik[52], Denise Harold[71], Giancarlo Russo[72], David C Rubinsztein[73,74], Anthony Bayer[75], Magda Tsolaki[76,77], Petra Proitsi[78], Nick C Fox[79,6], Harald Hampel[80,81,82], Michael J Owen[83,84], Simon Mead[85], Peter Passmore[86], Kevin Morgan[87], Martin Rossor[88], Michelle Lupton[89,90], Per Hoffmann[91,92,93,94], Johannes Kornhuber[95], Brian Lawlor[96], Andrew McQuillin[97], Ammar Al-Chalabi[98,99], Joshua C Bis[100], Agustin Ruiz[101,102], Mercè Boada[103], Sudha Seshadri[104,105,106], Alexa Beiser[107,108,106], Kenneth Rice[109], Sven van der Lee[110], Philip L. De Jager[111], Daniel H. Geschwind[112,113,114], Matthias Riemenschneider[115], Steffi Riedel-Heller[116], Jerome I Rotter[117], Gerhard Ransmayr[118], Bradley T. Hyman[11,12], Carlos Cruchaga[120], Montserrat Alegret[121], Bendik Winsvold[122,123], Priit Palta[124], Kai-How Farh[125,3], Ester Cuenca-Leon[2,3,12], Nicholas Furlotte[126], Tobias Kurth[127], Lannie Ligthart[128], Gisela Terwindt[129], Tobias Freilinger[130,131], Caroline Ran[132], Scott Gordon[89], Guntram Borck[133], Hieab Adams[110,134], Terho Lehtimäki[135,136], Juho Wedenoja[137,138], Julie Buring[139], Markus Schürks[140], Maria Hrafnsdottir[141], Jouke-Jan Hottenga[128,142], Brenda Penninx[143], Ville Artto[144], Mari Kaunisto[124], Salli Vepsäläinen[144], Nicholas Martin[89], Grant Montgomery[145], Mitja Kurki[1,3,13,124], Eija Hämäläinen[124], Hailiang Huang[1,2,146], Jie Huang[147,148], Cynthia Sandor[149], Caleb Webber[149], Bertram Muller-Myhsok[150,151,152], Stefan Schreiber[153,154], Veikko Salomaa[155], Elizabeth Loehrer[156], Hartmut Göbel[157], Alfons Macaya[158], Patricia Pozo-Rosich[159,160], Thomas Hansen[161,162], Thomas Werge[162,163,164], Jaakko Kaprio[124,138], Andres Metspalu[165], Michel Ferrari[166], Andrea Belin[167], Arn Maagdenberg[168,166], John-Anker Zwart[169], Dorret Boomsma[170,128], Nicholas Eriksson[126], Jes Olesen[161], Daniel Chasman[171,12], Dale Nyholt[172], Andreja Avbersek[173], Larry Baum[174], Samuel Berkovic[175], Jonathan Bradfield[176], Russell Buono[177,178,179], Claudia B. Catarino[173,180], Patrick Cossette[181], Peter Jonghe[182,183,184], Chantal Depondt[185], Dennis Dlugos[186,187], Thomas Ferraro[188], Jacqueline French[189], Helle Hjalgrim[190], Jennifer Jamnadas-Khoda[173,191], Reetta Kälviäinen[192,193], Wolfram Kunz[194,195], Holger Lerche[196], Costin Leu[197], Dick Lindhout[198,199], Warren Lo[200,201], Daniel Lowenstein[202], Mark McCormack[203,204], Rikke Møller[205,206], Anne Molloy[207], Ping-Wing Ng[208,209], Karen Oliver[210], Michael Privitera[211,212], Rodney Radtke[213], Ann-Kathrin Ruppert[214], Thomas Sander[214], Steven Schachter[215,11,12], Christoph Schankin[216,217], Ingrid Scheffer[218,219,220], Susanne Schoch[221], Sanjay Sisodiya[222,223], Philip Smith[224], Michael Sperling[225], Pasquale Striano[226], Rainer Surges[227,228], Neil G. Thomas[229], Frank Visscher[230], Christopher D. Whelan[203], Federico Zara[231], Erin Heinzen[232], Anthony Marson[233,234], Felicitas Becker[235], Hans Stroink[236],

Fritz Zimprich[237], Thomas Gasser[238,239], Raphael Gibbs[240], Peter Heutink[239,238], Maria Martinez[241,242], Huw Morris[222], Manu Sharma[243], Mina Ryten[222], Boniface Mok[244,245], Sara Pulit[246,247,3], Steve Bevan[248], Elizabeth Holliday[249], John Attia[250,251], Thomas Battey[252,253], Giorgio Boncoraglio[254,255], Vincent Thijs[220,256], Wei-Min Chen[257], Braxton Mitchell[258,259], Peter Rothwell[260], Pankaj Sharma[261,262], Cathie Sudlow[263], Astrid Vicente[264,265], Hugh Markus[266], Christina Kourkoulis[252,3], Joana Pera[267], Miriam Raffeld[268,119], Scott Silliman[269], Vesna Boraska Perica[270], Laura M. Thornton[271], Laura M. Huckins[272], N. William Rayner[273,274,275], Cathryn M. Lewis[276], Monica Gratacos[277], Filip Rybakowski[278], Anna Keski-Rahkonen[279], Anu Raevuori[280,279], James I. Hudson[281], Ted Reichborn-Kjennerud[282,283], Palmiero Monteleone[284], Andreas Karwautz[285], Katrin Mannik[165,286], Jessica H. Baker[271], Julie K. O'Toole[287], Sara E. Trace[288], Oliver S. P. Davis[289], Sietske Helder[290,276], Stefan Ehrlich[291], Beate Herpertz-Dahlmann[292], Unna N. Danner[293], Annemarie A. van Elburg[293,294], Maurizio Clementi[295], Monica Forzan[296], Elisa Docampo[297,298], Jolanta Lissowska[299], Joanna Hauser[300], Alfonso Tortorella[301], Fragiskos Gonidakis[302], Konstantinos Tziouvas[303], Hana Papezova[304,305], Zeynep Yilmaz[271], Gudrun Wagner[306], Sarah Cohen-Woods[307], Stefan Herms[309,308,91], Antonio Julia[310], Raquel Rabionet[311,312,313,314], Danielle M. Dick[315], Samuli Ripatti[124,138,316], Ole A. Andreassen[317,318], Thomas Espeseth[317,319,320], Astri Lundervold[321,320], Vidar M. Steen[317,322], Dalila Pinto[323,324,325,326], Stephen W. Scherer[328,329], Harald Aschauer[330], Alexandra Schosser[331,332], Lars Alfredsson[333], Leonid Padyukov[334,335], Katherine A. Halmi[336], James Mitchell[337,338], Michael Strober[339], Andrew W. Bergen[340,341], Walter Kaye[342], Jin Peng Szatkiewicz[271], Bru Cormand[312,312,313,343], Josep Antoni Ramos-Quiroga[344,345,347,346], Cristina Sánchez-Mora[345,344,347], Marta Ribasés[345,344,347], Miguel Casas[348,349,344,350], Amaia Hervas[351], Maria Jesús Arranz[352], Jan Haavik[353,354], Tetyana Zayats[353,1], Stefan Johansson[355,322], Nigel Williams[75], Astrid Dempfle[356], Aribert Rothenberger[357], Jonna Kuntsi[358], Robert D. Oades[359], Tobias Banaschewski[360], Barbara Franke[361,362,363], Jan K. Buitelaar[364,365], Alejandro Arias Vasquez[366], Alysa E. Doyle[119,12], Andreas Reif[367], Klaus-Peter Lesch[368,369,370], Christine Freitag[371], Olga Rivero[372], Haukur Palmason[141], Marcel Romanos[373], Kate Langley[374,83], Marcella Rietschel [375], Stephanie H Witt[375], Soeren Dalsgaard[376,164,377], Anders Børglum[378,164,379,380], Irwin Waldman[381], Beth Wilmot[382], Nikolas Molly [383], Claiton Bau[384,385], Jennifer Crosbie[386,387], Russell Schachar[388,387], Sandra K. Loo[389], James J. McGough[390], Eugenio Grevet[385,392], Sarah E. Medland[89], Elise Robinson[1,2,5], Lauren Weiss[393,394,395], Elena Bacchelli[396], Anthony Bailey[397,398], Vanessa Bal[393,394,395], Agatino Battaglia[399], Catalina Betancur[400], Patrick Bolton[358,401], Rita Cantor[402], Patrícia Celestino-Soper[403], Geraldine Dawson[404], Silvia De Rubeis[323,324,407], Frederico Duque[406,405], Andrew Green[408,409], Sabine M. Klauck[410], Marion Leboyer[411,412,413], Pat Levitt[414,65], Elena Maestrini[415], Shrikant Mane[416,417], Daniel Moreno-De-Luca[418], Jeremy Parr[419,420,421], Regina Regan[409,422], Abraham Reichenberg[272], Sven Sandin[323,324,423], Jacob Vorstman[424,425], Thomas Wassink[426], Ellen Wijsman[427,109], Edwin Cook[428], Susan Santangelo[430,431], Richard Delorme[432,433], Bernadette Rogé[434,435], Tiago Magalhaes[422,436], Dan Arking[437], Thomas G Schulze[438,439,375,440,441], Robert C Thompson[442,443], Jana Strohmaier[375,444], Keith Matthews[445,446], Ingrid Melle[447,448], Derek Morris[449], Douglas Blackwood[450], Andrew McIntosh[450], Sarah E Bergen[423], Martin Schalling[451,452], Stéphane Jamain[411,412,413], Anna Maaser[92,91], Sascha B Fischer[94,93], Céline S Reinbold[94,93], Janice M Fullerton[454,455], José G Guzman-Parra[456,457], Fermin Mayoral[456,457], Peter R Schofield[454,455], Sven Cichon[458,93,460], Thomas W Mühleisen[460,94], Franziska Degenhardt[461], Johannes Schumacher[461], Michael Bauer[462], Philip B Mitchell[463,464], Elliot S Gershon[465], John Rice[466], James B Potash[440], Peter P Zandi[467], Nick Craddock[83], I Nicol Ferrier[419], Martin Alda[468,469], Guy A. Rouleau[470,471], Gustavo Turecki[472], Roel Ophoff[474,475], Carlos Pato[476], Adebayo Anjorin[473], Eli Stahl[272,316],

Markus Leber[477], Piotr M Czerski[478], Cristiana Cruceanu[479,480], Ian R Jones[481], Danielle Posthuma[482,483], Till Andlauer[150,484], Andreas J Forstner[461,91,94,486,93], Fabian Streit[375], Bernhard T. Baune[487], Tracy Air[487], Grant Sinnamon[489,490], Naomi Wray[145,488], Donald MacIntyre[491], David Porteous[492], Georg Homuth[493], Margarita Rivera[494,276], Jakob Grove[164,379,378,495], Christel Middeldorp[496,497,128], Ian Hickie[498], Michele Pergadia[120], Divya Mehta[499,500], Johannes H Smit[143,502,503], Rick Jansen[143], Eco de Geus[128,502], Erin Dunn[13,501], Qingqin Li[504], Matthias Nauck[505,506], Robert A Schoevers[507], Aartjan TF Beekman[143,508], James A. Knowles[509], Alexander Viktorin[423], Paul Arnold[510,511,425], Cathy Barr[512,388,387], Gabriel Bedoya-Berrio[513], O. Bienvenu[514], Helena Brentani[515], Christie Burton[388], Beatriz Camarena[516], Carolina Cappi[515], Danielle Cath[517,518], Maria Cavallini[519], Daniele Cusi[520], Sabrina Darrow[521], Damiaan Denys[523,524], Eske Derks[89], Andrea Dietrich[517,525], Thomas Fernandez[522], Martijn Figee[523], Nelson Freimer[474], Gloria Gerber[13], Marco Grados[440], Erica Greenberg[119], Andreas Hartmann[526,527,528], Matthew Hirschtritt[393], Pieter Hoekstra[525], Alden Huang[529,390], Chaim Huyser[530,531], Cornelia Illmann[119], Michael Jenike[12], Samuel Kuperman[532], Bennett Leventhal[521], Christine Lochner[533], Gholson Lyon[534], Fabio Macciardi[535], Marcos Madruga-Garrido[537], Irene A. Malaty[536], Athanasios Maras[538], Lauren McGrath[539], Euripedes Miguel[540], Pablo Mir[541,542], Humberto Nicolini[543,544], Michael S. Okun[545,546,547], Andrew Pakstis[417], John Piacentini[390], Christopher Pittenger[548], Kerstin Plessen[549,550], Vasily Ramensky[551], Eliana M. Ramos[552], Victor Reus[393,395], Margaret Richter[553,554], Mark Riddle[514], Mary Robertson[555], Veit Roessner[556], Maria Rosário[557,558], Paul Sandor[554,559,560], Dan Stein[561,533], Fotis Tsetsos[562], Filip Van Nieuwerburgh[563], Sarah Weatherall[13], Jens Wendland[564], Tomasz Wolanczyk[565], Yulia Worbe[566,567,568], Fernando Goes[440], Nicole McLaughlin[569,570], Paul. S Nestadt[440], Hans-Jorgen Grabe[571], Christel Depienne[572,573,574], Anuar Konkashbaev[575], Nuria Lanzagorta[576], Ana Valencia-Duarte[577,578], Elvira Bramon[97], Nancy Buccola[579], Wiepke Cahn[580], Murray Cairns[581,582,583], Siow Chong[584], David Cohen[585,586], Benedicto Crespo-Facorro[587,347], James Crowley[288], Michael Davidson[588,589], Lynn DeLisi[590,12], Timothy Dinan[591,592], Gary Donohoe[593], Elodie Drapeau[272,323,324], Jubao Duan[594,595], Lieuwe Haan[523,596], David Hougaard[597], Sena Karachanak-Yankova[598], Andrey Khrunin[599], Janis Klovins[600], Vaidutis Kucinskas[601], Jimmy Lee Chee Keong[602], Svetlana Limborska[603], Carmel Loughland[604,250], Jouko Lönnqvist[155,605], Brion Maher[514], Manuel Mattheisen[606,607,608], Colm McDonald[609,610], Kieran Murphy[611], Igor Nenadic[612,613], Jim Os[580,614,615], Christos Pantelis[616,617], Michele Pato[476], Tracey Petryshen[2,13], Digby Quested[618,619], Panos Roussos[272], Alan Sanders[620,595], Ulrich Schall[250], Sibylle Schwab[621], Kang Sim[622,623], Hon-Cheong So[624,625,626], Elisabeth Stögmann[237], Mythily Subramaniam[584,623], Draga Toncheva[598,627], John Waddington[203], James Walters[83,84], Wei Cheng[271], Robert Cloninger[628], David Curtis[629,630], Frans Henskens[631,632,251], Morten Mattingsdal[447,633], Sang-Yun Oh[634,635], Rodney Scott[250,251,636], Bradley Webb[637], Claire Churchhouse[1,2,3], Gerome Breen[638,639], Cynthia Bulik[640,423], Mark Daly[1,2,3], Martin Dichgans[14,151], Stephen V. Faraone[641], Rita Guerreiro[6,7], Peter Holmans[8], Kenneth Kendler[642], Bobby Koeleman[643], Carol A. Mathews[644], Alkes Price[3,5], Jeremiah Scharf[2,3,10,13,645,11,12], Pamela Sklar[272], Julie Williams[9], Nick Wood[244,646,629], Chris Cotsapas[3,647], Aarno Palotie[1,2,3,13,11,12,124], Jordan Smoller[2,13], Patrick Sullivan[640,648], Jonathan Rosand[3,10,11,12], Aiden Corvin†*[2,649], Benjamin M. Neale†*[3,1,2,3], on behalf of the Brainstorm consortium

Affiliations:

1) Analytic and Translational Genetics Unit, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA

2) Stanley Center for Psychiatric Research, Broad Institute of MIT and Harvard, Cambridge, Massachusetts, USA

3) Program in Medical and Population Genetics, Broad Institute of MIT and Harvard, Cambridge, Massachusetts, USA

4) Department of Mathematics, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA

5) Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA

6) UK Dementia Research Institute, University College London, London, UK
7) Department of Molecular Neuroscience, Institute of Neurology, University College London, London, UK
8) Department of Psychiatry and Behavioral Science, Stanford University, Stanford, California, USA
9) Cardiff University, Medical Research Council Center for Neuropsychiatric Genetics & Genomics, Institute of Psychology, Medicine & Clinical Neuroscience, Cardiff, UK
10) Center for Human Genetic Research, Massachusetts General Hospital, Boston, MA, USA
11) Department of Neurology, Massachusetts General Hospital, Boston, MA, USA
12) Harvard Medical School, Boston, MA, USA
13) Psychiatric and Neurodevelopmental Genetics Unit (PNGU), Center for Human Genetics Research, Massachusetts General Hospital, Boston, MA, USA
14) Institute for Stroke and Dementia Research (ISD), University Hospital, LMU Munich, Munich, Germany
15) Department of Neurology, Brigham & Women's Hospital, Harvard Medical School, Boston, MA, USA
16) Charite Universitatsmedizin Berlin, Berlin, Germany
17) Department of Computer Science, New Jersey Institute of Technology, New Jersey, USA
18) INSERM U1167 LabEx DISTALZ, Lille, France
19) Institut Pasteur de Lille, U1167, Lille, France
20) Université de Lille, U1167, RID-AGE, Risk Factors and Molecular Determinants of Aging-Related Diseases, Lille, France
21) Centre Hosp. Univ Lille, Lille, France
22) Laboratory for Statistical Analysis, RIKEN Center for Integrative Medical Sciences
23) Center for Genomic Medicine, Kyoto University Graduate School of Medicine, Kyoto, Japan
24) INSERM U1061 - Neuropsychiatry: Epidemiological and Clinical Research, Montpellier, France
25) University of Montpellier, Montpellier, France
26) Memory Research and Resources Center, Department of Neurology, Montpellier University Hospital Gui de Chauliac, Montpellier, France
27) INSERM, UMR 1219, Bordeaux, France
28) University of Bordeaux, Bordeaux, France
29) Rouen University Hospital, Rouen, France
30) Inserm U1245, Rouen, France
31) Centre National de Recherche en Génomique Humaine (CNRGH), Institut de biologie François Jacob, CEA, Evry, France
32) Department of Gerontology, Hôpital Broca, AH-HP, Paris, France
33) Hôpital Paul Brousse Université Paris Sud XI, Le Kremlin-Bicêtre, Paris, France
34) Gertrude H. Sergievsky Center and Dept of Neurology, Columbia University, New York, NY, USA
35) Columbia University, New York, NY, USA
36) Dept. of Neuroscience, Icahn School of Medicine at Mount Sinai, New York, NY, USA
37) Translational Genomics Research Institute, Neurogenomics Division, Phoenix, AZ, USA
38) University of Pittsburgh, Pittsburgh, PA, USA
39) Kaiser Permanente Washington Health Research Institute, Seattle, WA, USA
40) Department of Medicine, University of Washington, WA, USA
41) Tanz Centre for Research in Neurodegenerative Diseases, University of Toronto, Toronto, Canada
42) Cambridge Institute for Medical Research, University of Cambridge, Cambridge, UK
43) Center for Applied Genomics of The Children's Hospital of Philadelphia, Philadelphia, PA, USA
44) Division of Human Genetics, Children's Hospital of Philadelphia, Philadelphia, PA, USA
45) Department of Pediatrics, The Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA
46) National Alzheimer Coordinating Center (NACC), University of Washington, Seattle, WA, USA
47) Department of Medicine, Boston University School of Medicine, Boston, MA, USA
48) Rush Alzheimers Disease Center, Chicago, IL, USA
49) Department of Neurological Sciences, Rush Medical College, Chicago, IL, USA
50) Department of Behavioral Sciences, Rush Medical College, Chicago, IL, USA
51) Banner Sun Health Research Institute, Sun City, AZ, USA
52) Sanders-Brown Center on Aging, University of Kentucky, Lexington, KY, USA
53) Department of Pathology, Duke University School of Medicine, Durham, NC, USA
54) College of Medicine, University of Kentucky, Lexington, KY, USA
55) Department of Biology, Brigham Young University, Provo, UT, USA
56) Layton Aging & Alzheimer's Disease Center, Oregon Health & Science University, Portland, OR, USA
57) Lou Ruvo Center for Brain Health, Neurological Institute, Cleveland Clinic, Cleveland, OH, USA
58) Department of Neurology, School of Medicine, Emory University, Atlanta, GA, USA
59) Department of Pathology, University of Michigan Medical School, Ann Arbor, MI, USA
60) University of New Mexico Health Sciences Center, Albuquerque, NM, USA
61) Institute for Memory Impairments and Neurological Disorders, University of California, Irvine, CA, USA

62) Department of Neurology, Oregon Health and Science University, Portland, OR, USA
63) Department of Neurology and Parkinson's Disease Research Education and Clinical Care Center (PADRECC), Portland Veterans Affairs Medical Center, Portland, OR, USA
64) Indiana Alzheimer Disease Center, Indiana University School of Medicine, Indianapolis, IN, USA
65) Keck School of Medicine of the University of Southern California, Los Angeles, CA, USA
66) Byrd Alzheimer's Institute, University of South Florida, Tampa, FL, USA
67) Department of Pathology, University of Utah, Salt Lake City, UT, USA
68) Department of Pathology, University of Washington, Seattle, WA, USA
69) Boston University School of Medicine, Boston, MA, USA
70) Department of Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, USA
71) School of Biotechnology, Dublin City University, Glasnevin, Dublin, Ireland
72) Functional Genomics Center Zurich, ETH/UZH-Zurich, Zurich, Switzerland
73) Department of Medical Genetics, Cambridge Institute for Medical Research, Cambridge, UK
74) UK Dementia Research Institute, Cambridge, UK
75) School of Medicine, Cardiff University, Cardiff, UK
76) 1st and 3rd Departments of Neurology, Aristotle University of Thessaloniki, Thessaloniki, Greece
77) Greek Association of Alzheimer's Disease and Related Disorders, Thessaloniki, Greece
78) Maurice Wohl Clinical Neuroscience Institute, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
79) Dementia Research Centre, UCL Institute of Neurology, London, UK
80) Sorbonne University, Paris, France
81) Department of Neurology, Institute for Memory and Alzheimer' Disease (IM2A), Hôpital Pitié-Salpêtrière, Paris, France
82) Brain and Spine Institute (ICM), Paris, France
83) MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, Cardiff, UK
84) Institute of Psychological Medicine and Clinical Neurosciences, School of Medicine, Cardiff University, Cardiff, UK
85) Institute of Prion Diseases and MRC Prion Unit, University College London, London, UK
86) Centre for Public Health, Queens University Belfast, Belfast, UK
87) University of Nottingham, Nottingham, UK
88) Department of Neurodegeneration, UCL Institute of Neurology, London, UK
89) QIMR Berghofer Medical Research Institute, Brisbane, Australia
90) Institute of Psychiatry Psychology and Neuroscience, Kings College London, UK
91) Department of Genomics, Life & Brain Center, University of Bonn, Bonn, Germany
92) Institute of Human Genetics, School of Medicine, University of Bonn & University Hospital Bonn, Bonn, Germany
93) Institute of Medical Genetics and Pathology, University Hospital Basel, Basel, Switzerland
94) Human Genomics Research Group, Department of Biomedicine, University of Basel, Basel, Switzerland
95) Department of Psychiatry and Psychotherapy, Friedrich-Alexander-Universität Erlangen-Nürnberg University Hospital, Erlangen, Germany
96) Department of Psychiatry, Trinity College, Dublin, Ireland
97) Division of Psychiatry, Molecular Psychiatry Laboratory,University College London, London, UK
98) Maurice Wohl Clinical Neuroscience Institute, Department of Basic and Clinical Neuroscience, King's College London, London, UK
99) King's College Hospital, London, UK
100) Cardiovascular Health Research Unit, Department of Medicine, University of Washington, Seattle, WA, USA
101) Research Center and Memory Clinic of Fundació ACE, Institut Català de Neurociències Aplicades, Barcelona, Spain
102) Facultat de Medicina i Ciències de la Salut, Universitat Internacional de Catalunya (UIC), Barcelona, Spain
103) Fundació ACE, Universitat Internacional de Catalunya, Barcelona, Spain
104) Glenn Biggs Institute for Alzheimer's and Neurodegenerative Diseases, University of Texas Health Sciences Center, San Antonio, Texas, USA
105) Neurology and Neurogenetics Core, Framingham Heart Study, Framingham, MA, USA
106) School of Medicine, Boston University, Boston, MA, USA
107) School of Public Health, Boston University, Boston, MA, USA
108) Framingham Heart Study, Framingham, MA, USA
109) Department of Biostatistics, University of Washington, Seattle, WA, USA
110) Department of Epidemiology, Erasmus Medical Centre, Rotterdam, the Netherlands
111) Center for Translational & Computational Neuroimmunology, Columbia University Medical Center, New York, NY, USA
112) Neurogenetics Program, Departments of Neurology and Human Genetics, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, USA
113) Center for Autism Research and Treatment, Semel Institute, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA, USA
114) Institute for Precision Health, University of California, Los Angeles, Los Angeles, CA, USA
115) Department of Psychiatry, Saarland University Hospital, Homburg, Germany
116) Institute of Social Medicine, Occupational Health and Public Health (ISAP), University of Leipzig, Leipzig, Germany
117) Institute for Translational Genomics and Population Sciences, Departments of Pediatrics and Medicine, LABioMed at Harbor-UCLA Medical Center, Torrance, CA, USA

118) Department of Neurology II, Kepler University Clinic, Johannes Kepler University, Linz, Austria
119) Massachusetts General Hospital, Boston, MA, USA
120) Washington University School of Medicine, St. Louis, MO, USA
121) Fundació ACE. Institut Català de Neurociències Aplicades, Barcelona, Spain
122) Communication and Research Unit for Musculoskeletal Disorders (FORMI), Oslo University Hospital, Oslo, Norway
123) Department of Neurology, Oslo University Hospital, Oslo, Norway
124) Institute for Molecular Medicine Finland (FIMM), HiLIFE, University of Helsinki, Helsinki, Finland
125) Illumina Inc., San Diego, CA, USA
126) 23andMe Inc., Mountain View, CA, US
127) Institute of Public Health, Charité – Universitätsmedizin Berlin, Germany
128) Department of Biological Psychology, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands
129) Leiden University Medical Center, Department of Neurology, Leiden, The Netherlands
130) Institute for Stroke and Dementia Research, Klinikum der Universitaet Muenchen, Munich, Germany
131) Department of Neurology and Epileptology, Hertie Institute for Clinical Brain Research, University of Tuebingen, Tuebingen, Germany
132) Department of Neuroscience, Karolinska Institutet, Stockholm, Sweden
133) Institute of Human Genetics, University of Ulm, Ulm, Germany
134) Department of Radiology and Nuclear Medicine, Erasmus Medical Centre, Rotterdam, the Netherlands
135) Department of Clinical Chemistry, Faculty of Medicine and Life Sciences, University of Tampere, Finland
136) Fimlab Ltd., Tampere, Finland
137) Department of Ophthalmology, University of Helsinki and Helsinki University Hospital, Helsinki, Finland
138) Department of Public Health, University of Helsinki, Helsinki, Finland
139) Brigham and Women's Hospital, Boston, MA
140) Department of Neurology, University Hospital Essen, Germany
141) Landspitali National University Hospital, Reykjavik, Iceland
142) Avera Institute for Human Genetics, Sioux Falls, SD, USA
143) Department of Psychiatry, VU University Medical Center, Amsterdam, The Netherlands
144) Department of Neurology, Helsinki University Central Hospital, Helsinki, Finland
145) Institute for Molecular Bioscience, University of Queensland, Brisbane, Australia
146) Department of Medicine, Harvard Medical School, Boston, MA, USA
147) Boston VA Research Institute, Boston, MA, USA
148) Brigham Women's Hospital Division of Aging, Harvard Medical School, Boston, MA, USA
149) Department of Physiology, Anatomy and Genetics, University of Oxford, Oxford, UK
150) Max Planck Institute of Psychiatry, Munich, Germany
151) Munich Cluster for Systems Neurology (SyNergy), Munich, Germany
152) Institute of Translational Medicine, University of Liverpool, Liverpool, UK
153) Institute of Clinical Molecular Biology, Kiel University and University Hospital Schleswig-Holstein, Kiel, Germany
154) Clinic of Internal Medicine I, University Hospital Schleswig-Holstein, Kiel, Germany
155) National Institute for Health and Welfare, Helsinki, Finland
156) Department of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, MA, USA
157) Kiel Pain and Headache Center, Kiel, Germany
158) Pediatric Neurology Research Group, Vall d'Hebron Research Institute, Autonomous University of Barcelona, Barcelona, Spain
159) Headache Unit, Neurology Department, Hospital Vall d'Hebron, Barcelona, Spain
160) Headache Research Group, VHIR, Universitat Autónoma, Barcelona, Spain
161) Danish Headache Center, Rigshospitalet Glostrup and University of Copenhagen, Copenhagen, Denmark
162) Institute of Biological Psychiatry, Roskilde, Denmark
163) Department of Clinical Sciences, University of Copenhagen, Copenhagen, Denmark
164) Lundbeck Foundation Initiative for Integrative Psychiatric Research, iPSYCH, Aarhus, Denmark
165) Estonian Genome Center, Institute of Genomics, University of Tartu, Tartu, Estonia
166) Department of Neurology, Leiden University Medical Center, Leiden, The Netherlands
167) Karolinska Institutet, Stockholm, Sweden
168) Department of Human Genetics, Leiden University Medical Center, Leiden, The Netherlands
169) Division of Clinical Neuroscience, Oslo University Hospital and University of Oslo, Oslo, Norway
170) Netherlands Twin Register, Vrije Universiteit, Amsterdam, The Netherlands
171) Division of Preventive Medicine, Brigham and Women's Hospital, Boston, MA, USA
172) Statistical and Genomic Epidemiology Laboratory, Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Queensland, Australia
173) Department of Clinical and Experimental Epilepsy, UCL Institute of Neurology, London, UK

174) Centre for Genomic Sciences, University of Hong Kong, Hong Kong
175) Epilepsy Research Centre, University of Melbourne, Heidelberg, Australia
176) Quantinuum Research LLC, San Diego, CA, USA
177) Cooper Medical School of Rowan University, Camden, NJ, USA
178) Thomas Jefferson University Hospital, Philadelphia, PA, USA
179) Children's Hospital of Philadelphia, Philadelphia, PA, USA
180) Epilepsy Society, Chalfont-St-Peter, Bucks, UK
181) Centre de Recherche du Centre Hospitalier de l'Universite de Montreal and Department of Neurosciences, Université de Montréal, Montréal, Canada
182) Neurogenetics Group, VIB-CMN, Antwerp, Belgium
183) University of Antwerp, Antwerp, Belgium
184) Department of Neurology, Antwerp University Hospital, Antwerp, Belgium
185) Department of Neurology, Hôpital Erasme, Université Libre de Bruxelles, Brussels, Belgium
186) Division of Neurology, Children's Hospital of Philadelphia, Philadelphia, PA, USA
187) Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA
188) Department of Biomedical Sciences, Cooper Medical School of Rowan University, Camden, NJ, USA
189) NYU School of Medicine, New York, NY, USA
190) Amplexa Genetics A/S, Odense, Denmark
191) Institute of Mental Health, University of Nottingham, Nottingham, UK
192) Epilepsy Center/Neurocenter, Kuopio University Hospital, Kuopio, Finland
193) Institute of Clinical Medicine, School of Medicine, Faculty of Health Sciences, University of Eastern Finland, Kuopio, Finland
194) Department of Epileptology, University Bonn Medical Center, Bonn, Germany
195) Institute of Experimental Epileptology and Cognition Research, University Bonn Medical Center, Bonn, Germany
196) Dept. of Neurology and Epileptology, Hertie Institute for Clinical Brain Research, University of Tübingen, Tübingen, Germany
197) Department of Clinical and Experimental Epilepsy, NIHR University College London Hospitals Biomedical Research Centre, UCL Institute of Neurology, London
198) Department of Genetics, University Medical Center Utrecht, the Netherlands
199) Epilepsy Foundation in the Netherlands (SEIN), Heemstede, the Netherlands
200) Departments of Pediatrics and Neurology, Ohio State University, Columbus, OH, USA
201) Nationwide Children's Hospital, Columbus, OH, USA
202) Department of Neurology, University of California, San Francisco, CA, USA
203) Department of Molecular and Cellular Therapeutics, Royal College of Surgeons in Ireland, Dublin, Ireland
204) Center for Molecular Medicine, University Medical Center Utrecht, Utrecht, the Netherlands
205) Danish Epilepsy Centre, Filadelfia, Dianalund, Denmark
206) Institute for Regional Health Services, University of Southern Denmark, Odense, Denmark
207) Trinity College Dublin, Dublin, Ireland
208) United Christian Hospital, Hong Kong
209) Hong Kong Sanatorium and Hospital, Hong Kong
210) Epilepsy Research Centre, University of Melbourne, Austin Health, Heidelberg, Australia
211) Department of Neurology, University of Cincinnati, Cincinnati, OH, USA
212) UC Gardner Neuroscience Institute, Cincinnati, OH, USA
213) Department of Neurology, Duke University School of Medicine, Durham, NC, USA
214) Cologne Center for Genomics (CCG), University of Cologne, Cologne, Germany
215) Department of Neurology, Beth Israel Deaconess Medical Center, Boston, MA, USA
216) Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Switzerland
217) Department of Neurology, University of Munich Hospital, Grosshadern, University of Munich, Germany
218) Department of Medicine, The University of Melbourne, Austin Health, Melbourne, Victoria, Australia
219) Department of Paediatrics, Royal Children's Hospital, The University of Melbourne, Melbourne, Victoria, Australia
220) Florey Institute of Neuroscience and Mental Health, Melbourne, Victoria, Australia
221) Institute of Neuropathology, Bonn University Medical School, Bonn, Germany
222) UCL Institute of Neurology, London, UK
223) Chalfont Centre for Epilepsy, Bucks, UK
224) University Hospital of Wales, Cardiff, UK
225) Department of Neurology, Thomas Jefferson University Hospital, Philadelphia, PA, USA
226) Pediatric Neurology and Muscular Diseases Unit-Department of Neurosciences, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health University of Genoa, "G. Gaslini" Institute, Genova, Italy
227) Department of Epileptology, University Hospital Bonn, Bonn, Germany
228) Section of Epileptology, Department of Neurology, University Hospital RWTH Aachen, Aachen, Germany

229) Institute of Applied Health Research, University of Birmingham, UK
230) Department of Neurology, Admiraal De Ruyter Hospital, Goes, The Netherlands
231) Laboratory of Neurogenetics, G. Gaslini Institute, Genova, Italy
232) Institute for Genomic Medicine, Columbia University Medical Center, New York, NY, USA
233) University of Liverpool, Liverpool, UK
234) Walton Centre NHS Foundation Trust, Liverpool, UK
235) Department of Neurology and Epileptology, University Hospital Tuebingen, Tuebingen, Germany
236) CWZ Hospital, Nijmegen, Netherlands
237) Department of Neurology, Medical University of Vienna, Austria
238) Hertie-Institute for Clinical Brain Research, University of Tübingen, Tübingen, Germany
239) German Center for Neurodegenerative Diseases (DZNE), Tübingen, Germany
240) Laboratory of Neurogenetics, National Institute on Aging, National Institutes of Health, Bethesda, MD, USA
241) INSERM U1220, IRSD, Toulouse, France
242) Université Paul Sabatier, Toulouse, France
243) Centre for Genetic Epidemiology, Institute for Clinical Epidemiology and Applied Biometery, University of Tubingen, Germany
244) Department of Molecular Neuroscience, Institute of Neurology, University College London, London, UK
245) Division of Life Science, Hong Kong University of Science and Technology, Hong Kong Special Administrative Region, China
246) Department of Genetics, Center for Molecular Medicine, University Medical Center Utrecht, Utrecht, The Netherlands
247) Big Data Institute, Li Ka Shing Centre for Health Information and Discovery, University of Oxford, Oxford, UK
248) University of Lincoln, Lincoln, UK
249) Faculty of Health and Medicine, University of Newcastle, Callaghan, Australia
250) University of Newcastle, Callaghan, Australia
251) Hunter Medical Research Institute, Newcastle, Australia
252) Center for Genomic Medicine, Massachusetts General Hospital, Boston, MA, USA
253) Division of Neurocritical Care and Emergency Neurology, Massachusetts General Hospital, Boston, MA, USA
254) Department of Cerebrovascular Diseases, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milano, Italy
255) University Milano-Bicocca, Monza, Italy
256) Austin Health, Heidelberg, Australia
257) University of Virginia Center for Public Health Genomics, University of Virginia, Charlottesville, VA, USA
258) Dept of Medicine, University of Maryland School of Medicine, Baltimore, MD, USA
259) Geriatrics Research and Education Clinical Center, Baltimore Veterans Administration Medical Center, Baltimore, MD, USA
260) Centre for Prevention of Stroke and Dementia, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK
261) Institute of Cardiovascular Research, Royal Holloway University of London, London, UK
262) Ashford & St Peters NHS Foundation Trust, Surrey, UK
263) University of Edinburgh, Edinburgh, UK
264) Instituto Nacional de Saúde Doutor Ricardo Jorge, Lisboa, Portugal
265) Biosystems and Integrative Sciences Institute - BioISI, University of Lisboa, Lisboa, Portugal
266) Department of Clinical Neurosciences, University of Cambridge, Cambridge, UK
267) Department of Neurology, Jagiellonian University Medical College, Kraków, Poland
268) The Warren Alpert Medical School of Brown University, Providence, RI, USA
269) Department of Neurology, College of Medicine-Jacksonville, University of Florida, Jacksonville, FL, USA
270) University of Split School of Medicine, Split, Croatia
271) University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
272) Icahn School of Medicine at Mount Sinai, New York, NY, USA
273) Wellcome Centre for Human Genetics, Nuffield Department of Medicine, University of Oxford, Oxford, UK
274) Oxford Centre for Diabetes, Endocrinology and Metabolism, Nuffield Department of Medicine, University of Oxford, Oxford, UK
275) Department of Human Genetics, Wellcome Sanger Institute, Hinxton, Cambridgeshire, UK
276) MRC Social, Genetic and Developmental Psychiatry Centre, King's College London, London, UK
277) Genes and Disease Programme, Centre for Genomic Regulation (CRG), Barcelona, Spain
278) Department of Adult Psychiatry, Poznan University of Medical Sciences, Poland
279) Clinicum, Department of Public Health, University of Helsinki, Finland
280) Department of Adolescent Psychiatry, Helsinki University Central Hospital, Helsinki, Finland
281) Harvard Medical School/McLean Hospital, Belmont, MA, USA
282) Norwegian Institute of Public Health, Oslo, Norway
283) University of Oslo, Oslo, Norway
284) Department of Medicine, Surgery and Dentistry “Scuola Medica Salernitana”, University of Salerno,Italy

285) Eating Disorders Unit, Department of Child and Adolescent Psychiatry, Medical University of Vienna, Vienna, Austria
286) Center for Integrative Genomics, University of Lausanne, Lausanne, Switzerland
287) Kartini Clinic, Portland, OR, USA
288) Department of Psychiatry, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
289) MRC Integrative Epidemiology Unit and Bristol Medical School, University of Bristol, Bristol, UK
290) Zorg op Orde BV, Leidschendam, The Netherlands
291) Division of Psychological & Social Medicine and Developmental Neurosciences, Faculty of Medicine, Technischen Universität Dresden, Dresden, Germany
292) Department of Child & Adolescent Psychiatry & Psychosomatic Medicine of University Clinics, RWTH Aachen, Aachen, the Netherlands
293) Altrecht Eating Disorders Rintveld, Altrecht Mental Health Institute, Zeist, The Netherlands
294) Faculty of Social Sciences, University of Utrecht, Utrecht, the Netherlands
295) Medical Genetics Unit, Department SDB, University of Padova, Padova, Italy
296) UOC Genetica ed Epidemiologica Clinica Az. Ospedaliera, Padova, Italy
297) Department of Human Genetics, CHU Sart-Tilman, University of Liège, Liège, Belgium
298) Department of Rheumatology, CHU Sart-Tilman, University of Liège, Liège, Belgium
299) Department of Cancer Epidemiology and Prevention, Cancer Center and M. Sklodowska-Curie Institute of Oncology, Warsaw, Poland
300) Department of Psychiatry, University of Medical Sciences, Poznan, Poland
301) Department of Psychiatry, University of Perugia, Perugia, Italy
302) Eating Disorders Unit, 1st Psychiatric Department, National and Kapodistrian University of Athens, Athens, Greece
303) Aglaia Kyriakou Childrens Hospital, Athens, Greece
304) Eating Disorders Unit, Department of Psychiatry, First Faculty of Medicine, Charles University, Prague, Czech Republic
305) General University Hospital, Prague, Czech Republic
306) Medical University of Vienna, Austria
307) School of Psychology, Flinders University, Adelaide, Australia
308) Division of Medical Genetics, University Hospital Basel, Basel, Switzerland
309) Genomics Research Group, Department of Biomedicine, University of Basel, Basel, Switzerland
310) Vall d'Hebron Research Institute, Barcelona, Spain
311) Institut de Recerca Sant Joan de Déu, Barcelona, Spain
312) Institut de Biomedicina de la Universitat de Barcelona (IBUB), Barcelona, Spain
313) Department of Genetics, Microbiology & Statistics, Faculty of Biology, University of Barcelona, Barcelona, Spain
314) Centre for Genomic Regulation (CRG), Barcelona, Spain
315) Virginia Commonwealth University, Richmond, VA, USA
316) Broad Institute of MIT and Harvard, Cambridge, USA
317) NORMENT, Div. of Mental Health and Addiction, University of Oslo, Oslo, Norway
318) Oslo University Hospital, Oslo, Norway
319) Department of Psychology, University of Oslo, Norway
320) K.G. Jebsen Center for Neuropsychiatric Disorders, University of Bergen, Bergen, Norway
321) Department of Biological and Medical Psychology, University of Bergen, Bergen, Norway
322) Department of Medical Genetics, Haukeland University Hospital, Bergen, Norway
323) Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, NY, USA
324) Seaver Autism Center for Research and Treatment, Icahn School of Medicine at Mount Sinai, New York, NY, USA
325) Department of Genetics and Genomic Sciences, and Institute for Genomics and Multiscale Biology, Icahn School of Medicine at Mount Sinai, New York, NY, USA
326) The Mindich Child Health & Development Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA
327) Friedman Brain Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA
328) McLaughlin Centre and Department of Molecular Genetics, University of Toronto, Toronto, Canada
329) The Centre for Applied Genomics, Hospital for Sick Children, Toronto, Canada
330) Biopsychosocial Corporation, Vienna, Austria
331) Department of Psychiatry and Psychotherapy, Medical University of Vienna, Vienna, Austria
332) Zentren für Seelische Gesundheit, BBRZ-Med, Vienna, Austria
333) Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden
334) Rheumatology Unit, Department of Medicine, Solna, Sweden
335) Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden
336) Weill Cornell Medical College, New York, New York, USA
337) School of Medicine, University of North Dakota, Grand Forks, ND, USA
338) Neuropsychiatric Research Institute, Fargo, ND, USA
339) Department of Psychiatry & Biobehavioral Sciences, Semel Institute for Neuroscience & Human Behavior, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, CA, USA

340) BioRealm, Culver City, California, USA
341) Oregon Research Institute, Eugene, OR, USA
342) Department of Psychiatry, University of California San Diego, La Jolla, CA, USA
343) Centro de Investigación Biomédica en Red de Enfermedades Raras (CIBERER), Instituto de Salud Carlos III, Madrid, Spain
344) Department of Psychiatry, Hospital Universitari Vall d'Hebron, Barcelona, Spain
345) Psychiatric Genetics Unit, Group of Psychiatry, Mental Health and Addiction, Vall d'Hebron Research Institute (VHIR), Universitat Autònoma de Barcelona, Barcelona, Spain
346) Department of Psychiatry and Legal Medicine, Universitat Autònoma de Barcelona, Barcelona, Spain
347) Biomedical Network Research Centre on Mental Health (CIBERSAM), Instituto de Salud Carlos III, Madrid, Spain
348) Universitat Autònoma de Barcelona, Barcelona, Spain
349) Programa Corporatiu "Neurodevelopment Disorders along Life Span", Institut Català de la Salut, Barcelona, Spain
350) Clinica Galatea y PAIMM, Mental Health Program for Impaired Physicians, Barcelona, Spain
351) Child and Adolescent Mental Health Unit, Hospital Universitario Mútua de Terrassa, Barcelona, Spain
352) Hospital de la Santa Creu i Sant Pau, Barcelona, Spain
353) K.G. Jebsen Centre for Neuropsychiatric Disorders, Department of Biomedicine, University of Bergen, Norway
354) Division of Psychiatry, Haukeland University Hospital, Bergen, Norway
355) K.G. Jebsen Centre for Neuropsychiatric Disorders, Department of Clinical Science, University of Bergen, Norway
356) Institute of Medical Informatics and Statistics, Kiel University, Kiel, Germany
357) Child and Adolescent Psychiatry/Psychotherapy, University Medical Center, Goettingen, Germany
358) Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK
359) Clinic for Child and Adolescent Psychiatry and Psychotherapy, University of Duisburg-Essen, Essen, Germany
360) Child and Adolescent Psychiatry and Psychotherapy, Central Institute of Mental Health, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany
361) Department of Human Genetics, Radboud University Medical Center, Nijmegen, The Netherlands
362) Department of Psychiatry, Radboud University Medical Center, Nijmegen, The Netherlands
363) Donders Institute for Brain, Cognition and Behaviour, Radboud University, Nijmegen, The Netherlands
364) Department of Cognitive Neuroscience, Donders Institute for Brain, Cognition and Behavior, Radboud University Medical Centre, Nijmegen, The Netherlands
365) Karakter Child and Adolescent Psychiatry University Center, Nijmegen, The Netherlands
366) Department of Psychiatry & Human Genetics, Donders Institute for Brain, Cognition and Behaviour, Radboud University Medical Center, Nijmegen, The Netherlands
367) Department of Psychiatry, Psychosomatic Medicine and Psychotherapy, University Hospital Frankfurt, Frankfurt am Main, Germany
368) Laboratory of Psychiatric Neurobiology, Institute of Molecular Medicine, I.M. Sechenov First Moscow State Medical University, Moscow, Russia
369) Department of Translational Psychiatry, School for Mental Health and Neuroscience (MHeNS), Maastricht University, Maastricht, The Netherlands
370) Division of Molecular Psychiatry, Center of Mental Health, University of Wuerzburg, Germany
371) Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, University Hospital Frankfurt, Goethe University, Frankfurt am Main, Germany
372) Division of Molecular Psychiatry, Center of Mental Health, University of Wuerzburg, Wuerzburg, Germany
373) Center of Mental Health, Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, University Hospital of Wuerzburg, Wuerzburg, Germany
374) School of Psychology, Cardiff University, UK
375) Central Institute of Mental Health, Department of Genetic Epidemiology in Psychiatry, Medical Faculty Mannheim, University of Heidelberg, Mannheim, Germany
376) National Centre for Register-based Research, Aarhus University, Aarhus, Denmark
377) Hospital of Telemark, Kragerø, Norway
378) Department of Biomedicine and Human Genetics, Aarhus University, Aarhus, Denmark
379) Center for Integrative Sequencing (iSEQ), Aarhus University, Aarhus, Denmark
380) Aarhus Genome Center, Aarhus, Denmark
381) Department of Psychology, Emory University, Atlanta, GA, USA
382) Department of Medical Informatics and Clinical Epidemiology, Oregon Health & Science University, Portland, OR, USA
383) Department of Psychological and Brain Sciences, University of Iowa, Iowa City, IA, USA
384) Departamento de Genética, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil
385) ADHD Outpatient Clinic, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil
386) Neurosciences and Mental Health Program, Research Institute, Hospital for Sick Children, Toronto, Canada
387) University of Toronto, Toronto, Canada
388) Hospital for Sick Children, Toronto, Canada
389) Department of Psychiatry, University of California, Los Angeles, Los Angeles, California, USA
390) Semel Institute for Neuroscience & Human Behavior, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, CA, USA
391) ADHD Outpatient Clinic, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil
392) Department of Psychiatry, Faculdade de Medicina, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil
393) Department of Psychiatry, University of California, San Francisco, San Francisco, CA, USA
394) Institute for Human Genetics, University of California, San Francisco, San Francisco, CA, USA

395) Weill Institute for Neurosciences, University of California, San Francisco, San Francisco, CA, USA
396) Department of Pharmacy and Biotechnology, University of Bologna, Bologna, Italy
397) Department of Psychiatry, University of British Columbia, Vancouver, Canada
398) Institute of Mental Health, University of British Columbia, Vancouver, Canada
399) Stella Maris Clinical Research Institute for Child and Adolescent Neuropsychiatry, Pisa, Italy
400) Sorbonne Université, INSERM, CNRS, Neuroscience Paris Seine, Institut de Biologie Paris Seine, Paris, France
401) NIHR Biomedical Research Centre in Mental Health Maudsley Hospital, London, UK
402) Department of Human Genetics, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, CA, USA
403) LifeOmic, Indianapolis, IN, USA
404) Department of Psychiatry and Behavioral Sciences, Duke University, Durham, NC, USA
405) University Clinic of Pediatrics, Faculty of Medicine, University of Coimbra, Coimbra, Portugal
406) Child Developmental Center, Hospital Pediátrico, Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal
407) Mindich Child Health and Development Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA
408) Dept of Clinical Genetics, Our Lady's Children's Hospital, Crumlin, Dublin, Ireland
409) School of Medicine and Medical Science, University College Dublin, Dublin, Ireland
410) Division of Molecular Genome Analysis and Division of Cancer Genome Research, German Cancer Research Center (DKFZ), Heidelberg, Germany
411) Inserm U955, Psychiatrie Translationnelle, Créteil, France
412) Faculté de Médecine, Université Paris Est, Créteil, France
413) Fondation FondaMental, Créteil, France
414) Children's Hospital Los Angeles, Los Angeles, CA, USA
415) Dept. of Pharmacy and Biotechnology, University of Bologna, Bologna, Italy
416) Yale Center for Genome Analysis, Yale University, New Haven, CT, USA
417) Department of Genetics, Yale University School of Medicine, New Haven, CT, USA
418) Division of Child and Adolescent Psychiatry, Department of Psychiatry and Human Behavior, Brown University, Providence, RI, USA
419) Institute of Neuroscience, Newcastle University, Newcastle, UK
420) Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle, UK
421) Northumberland, Tyne & Wear NHS Foundation Trust, Northumberland, UK
422) Genomics Medicine Ireland, Dublin, Ireland
423) Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden
424) Department of Psychiatry, The Hospital for Sick Children and University of Toronto, Toronto, Canada
425) Program in Genetics and Genome Biology, Hospital for Sick Children, Toronto, Canada
426) Department of Psychiatry, Carver College of Medicine, University of Iowa, Iowa City, IA, USA
427) Division of Medical Genetics, Department of Medicine, University of Washington, Seattle, WA, USA
428) Department of Psychiatry, University of Illinois at Chicago, Chicago, IL, USA
429) Tufts University School of Medicine, Boston, MA, USA
430) Center for Psychiatric Research, Maine Medical Center Research Institute, Portland, ME, USA
431) Department of Psychiatry, Tufts University School of Medicine, Boston, MA, USA
432) Child and Adolescent Psychiatry Department, Robert Debre Hospital, APHP, Paris, France
433) Human Genetics and Cognitive Functions, Institut Pasteur, Paris, France
434) Centre d'Etudes et de Recherches en Psychopathologie et Psychologie de la Santé (CERPPS), Université Toulouse Jean Jaurès, Toulouse, France
435) CERESA, Toulouse, France
436) Academic Centre on Rare Diseases University College Dublin (ACoRD/UCD), Dublin, Ireland
437) McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA
438) Institute of Psychiatric Phenomics and Genomics (IPPG), University Hospital, LMU Munich, Munich, Germany
439) Department of Psychiatry and Psychotherapy, University Medical Center Göttingen, Göttingen, Germany
440) Department of Psychiatry and Behavioral Sciences, Johns Hopkins University, Baltimore, MD, USA
441) Human Genetics Branch, National Institute of Mental Health, National Institutes of Health, US Department of Health and Human Services, Bethesda, MD, USA
442) Molecular and Behavioral Neuroscience Institute, University of Michigan, Ann Arbor, MI, USA
443) Department of Psychiatry, University of Michigan, Ann Arbor, MI, USA
444) SRH University Heidelberg, Academy for Psychotherapy, Heidelberg, Germany
445) Division of Neuroscience, School of Medicine, University of Dundee, Dundee, UK
446) Advanced Interventions Service, NHS Tayside, Dundee, UK
447) NORMENT, K.G. Jebsen Centre for Psychosis Research, Institute of Clinical Medicine, University of Oslo, Oslo, Norway
448) Division of Mental Health and Addiction, Oslo University Hospital, Oslo, Norway
449) Cognitive Genetics and Cognitive Therapy Group, Neuroimaging, Cognition and Genomics (NICOG) Centre, School of Psychology and Discipline of Biochemistry, National University of Ireland Galway, Galway, Ireland

450) Division of Psychiatry, University of Edinburgh, Edinburgh, UK
451) Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden
452) Center for Molecular Medicine, Karolinska University Hospital, Stockholm, Sweden
453) Université Paris Est, Faculté de Médecine, Créteil, France
454) Neuroscience Research Australia, Sydney, Australia
455) School of Medical Sciences, University of New South Wales, Sydney, Australia
456) Unidad de Salud Mental, Hospital Regional Universitario de Malaga, Malaga, Spain
457) Instituto de Investigación Biomédica de Málaga (IBIMA), Malaga, Spain
458) Department of Biomedicine, University of Basel, Basel, Switzerland
459) Institute of Medical Genetics and Pathology, University Hospital Basel, Basel, Switzerland
460) Institute of Neuroscience and Medicine (INM-1), Research Center Juelich, Juelich, Germany
461) Institute of Human Genetics, University of Bonn, Bonn, Germany
462) Department of Psychiatry and Psychotherapy, University Hospital Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany
463) School of Psychiatry, University of New South Wales, Sydney, Australia
464) Black Dog Institute, Sydney, Australia
465) University of Chicago, Chicago, IL, USA
466) Washington University, St. Louis, MO, USA
467) Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA
468) Department of Psychiatry, Dalhousie University, Halifax, Canada
469) National Institute of Mental Health, Klecany, Czech Republic
470) Montreal Neurological Institute, McGill University, Montréal, Canada
471) Department of Neurology and Neurosurgery, McGill University, Montréal, Canada
472) Department of Psychiatry, McGill University, Montréal, Canada
473) University College London, London, UK
474) Center for Neurobehavioral Genetics, Semel Institute for Neuroscience & Human Behavior, University of California at Los Angeles, Los Angeles, CA, USA
475) UMC Utrecht, Utrecht, The Netherlands
476) SUNY Downstate Medical Center, Brooklyn, NY, USA
477) Hospital for Psychiatry and Psychotherapy, Cologne, Germany
478) Laboratory of Psychiatric Genetics, Department of Psychiatry, Poznan University of Medical Sciences, Poznan, Poland
479) Douglas Mental Health University Institute, McGill University, Montreal, Canada.
480) Department of Translational Research in Psychiatry, Max-Planck Institute of Psychiatry, Munich, Germany
481) National Centre for Mental Health, MRC Centre for Neuropsychiatric Genetics and Genomics, Cardiff University, Cardiff, UK
482) Department Complex Trait Genetics, Center for Neurogenomics and Cognitive Research, VU University, Amsterdam, The Netherlands
483) Department Clinical Genetics, VU University Medical Center, Amsterdam Neuroscience, Amsterdam, The Netherlands
484) Department of Neurology, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany
485) Institute of Human Genetics, University of Bonn, Bonn, Germany
486) Department of Psychiatry (UPK), University of Basel, Basel, Switzerland
487) Discipline of Psychiatry, University of Adelaide, Adelaide, Australia
488) Queensland Brain Institute, University of Queensland, Brisbane, Australia
489) Bela Menso Brain and Behaviour Centre, James Cook University, Varsity Lakes, Australia
490) Bond University, Faculty of Society and Design, Robina, Australia
491) Division of Psychiatry, Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK
492) Centre for Genomic and Experimental Medicine, University of Edinburgh, Edinburgh, UK
493) Interfaculty Institute for Genetics and Functional Genomics, University Medicine Greifswald, Greifswald, Germany
494) Department of Biochemistry and Molecular Biology II, Institute of Neurosciences, Center for Biomedical Research, University of Granada, Granada, Spain
495) Bioinformatics Research Centre, Aarhus University, Aarhus, Denmark
496) Child Health Research Centre, University of Queensland, Brisbane, Australia
497) Child and Youth Mental Health Service, Children's Health Queensland Health and Hospital Service, Brisbane, Australia
498) Brain and Mind Centre, University of Sydney, Sydney, Australia
499) School of Psychology and Counselling, Faculty of Health, Institute of Health and Biomedical Innovation, Queensland University of Technology, Queensland, Australia
500) University of Queensland, Brisbane, Australia
501) Department of Psychiatry, Harvard Medical School, Boston, MA, USA
502) Amsterdam Public Health Research Institute, VU Medical Center, Amsterdam, the Netherlands
503) Department of Research and Innovation, GGZ Ingeest, Specialized Mental Health Care, Amsterdam, the Netherlands
504) Janssen Research & Development LLC, Raritan, NJ, USA
505) Institute of Clinical Chemistry and Laboratory Medicine, University Medicine Greifswald, Greifswald, Germany

506) German Centre for Cardiovascular Research (DZHK e.V.), Partner Site Greifswald, Greifswald, Germany
507) Research School of Behavioural and Cognitive Neurosciences, Department of Psychiatry, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands
508) Department of Psychiatry GGZ INGEEST, Amsterdam, the Netherlands
509) Department of Cell Biology, SUNY Downstate Medical Center, Brooklyn, NY, USA
510) Mathison Centre for Mental Health Research & Education, Hotchkiss Brain Institute, Cumming School of Medicine, University of Calgary, Calgary, Canada
511) Departments of Psychiatry and Medical Genetics, Cumming School of Medicine, University of Calgary, Calgary, Canada
512) Krembil Research Institute, University Health Network, Toronto, Canada
513) Grupo de Genética Molecular, Instituto de Biología, Facultad de Ciencias Exactas y Naturales, Universidad de Antioquia, Medellín, Colombia
514) Johns Hopkins University School of Medicine, Baltimore, MD, USA
515) Department of Psychiatry, Sao Paulo Medical School, University of Sao Paulo, Sao Paulo, Brazil
516) Depto. Farmacogenética, Instituto Nacional de Psiquiatria Ramon de la Fuente Muñiz, Mexico City, Mexico
517) University of Groningen, Groningen, the Netherlands
518) GGz Drenthe and Department of Psychiatry, University Medical Center Groningen, Groningen, The Netherlands
519) Ospedale San Raffaele, Milano, Italy
520) Bio4Dreams Srl, Milan, Italy
521) University of California, San Francisco, CA, USA
522) Yale University School of Medicine, New Haven, CT, USA
523) Department of Psychiatry, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands
524) Netherlands Institute for Neuroscience, Royal Netherlands Academy of Arts and Sciences, Amsterdam, the Netherlands
525) Department of Child and Adolescent Psychiatry, University Medical Center Groningen, Groningen, The Netherlands
526) Centre National Maladie 'Syndrome Rare Gilles de la Tourette', Groupe Hospitalier Pitié-Salpêtrière, Paris, France
527) Assistance Publique-Hôpitaux de Paris, Département de Neurologie, Groupe Hospitalier Pitié-Salpêtrière, Paris, France
528) Sorbonne Universités, UPMC Université Paris 06, UMR S 1127, CNRS UMR 7225, ICM, Paris, France
529) Bioinformatics Interdepartmental Program, University of California, Los Angeles, Los Angeles, CA, USA
530) De Bascule, Amsterdam, The Netherlands
531) Department of Child and Adolescent Psychiatry, Academic Medical Center, University of Amsterdam, Amsterdam, the Netherlands
532) Carver College of Medicine, University of Iowa, Iowa City, IA, USA
533) MRC Unit on Risk and Resilience in Mental Disorders, Department of Psychiatry, University of Stellenbosch, Cape Town, South Africa
534) Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, USA
535) Department of Psychiatry and Human Behavior, University of California, Irvine, Irvine, CA, USA
536) Department of Neurology, University of Florida, Gainesville, FL, USA
537) Sección de Neuropediatría, Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Seville, Spain
538) Yulius Academy, Yulius Mental Health Organization, Barendrecht, The Netherlands
539) Department of Psychology, University of Denver, Denver, CO, USA
540) Sao Paulo Medical School, University of Sao Paulo, Sao Paulo, Brazil
541) Unidad de Trastornos del Movimiento, Servicio de Neurología y Neurofisiología Clínica, Instituto de Biomedicina de Sevilla, Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla, Seville, Spain
542) Centro de Investigación Biomédica en Red sobre Enfermedades Neurodegenerativas (CIBERNED), Madrid, Spain
543) National Institute of Genomic Medicine (INMEGEN), Ciudad de México, Mexico
544) Carracci Medical Group, Ciudad de México, Mexico
545) Departments of Neurology and Neurosurgery, University of Florida, Gainesville, FL, USA
546) Fixel Center for Neurological Diseases, University of Florida, Gainesville, FL, USA
547) McKnight Brain Institute, University of Florida, Gainesville, FL, USA
548) Department of Psychiatry, Yale School of Medicine, New Haven, CT, USA
549) Division of Adolescent and Child Psychiatry, Department of Psychiatry, Lausanne University Hospital, Lausanne, Switzerland
550) Child and Adolescent Mental Health Centre, Mental Health Services Capital Region Copenhagen, University of Copenhagen, Copenhagen, Denmark
551) Moscow Institute of Physics and Technology, Dolgoprudny, Institusky 9, Moscow, Russia
552) Department of Psychiatry, David Geffen School of Medicine, University of California at Los Angeles, Los Angeles, CA, USA
553) Frederick W. Thompson Anxiety Disorders Centre, Sunnybrook Health Sciences Centre, Toronto, Canada
554) Department of Psychiatry, University of Toronto, Toronto, Canada
555) Division of Neuropsychiatry, University College London, London, UK
556) Department of Child and Adolescent Psychiatry, Faculty of Medicine, Technischen Universität Dresden, Dresden, Germany
557) Child and Adolescent Psychiatry Unit (UPIA), Department of Psychiatry, Federal University of São Paulo, Brazil
558) Yale Child Study Center, Yale University School of Medicine, New Haven, CT, USA
559) University Health Network, University of Toronto, Toronto, Canada

560) Youthdale Treatment Centers, Toronto, Canada
561) Dept of Psychiatry, University of Cape Town, Cape Town, South Africa
562) Department of Molecular Biology and Genetics, Democritus University of Thrace, Alexandroupolis, Greece
563) Laboratory of Pharmaceutical Biotechnology, Ghent University, Ghent, Belgium
564) Pfizer, Inc., New York, NY, USA
565) Department of Child Psychiatry, Medical University of Warsaw, Warsaw, Poland
566) Sorbonne Université, Faculty of Médecine, Paris, France
567) Reference center for Gilles de la Tourette syndrome, Pitie-Salpetriere Hospital, Paris, France
568) Department of Physiology, Saint Antoine Hospital, Paris, France
569) Butler Hospital, Providence, RI, USA
570) Alpert Medical School of Brown University, Providence, RI, USA
571) Department of Psychiatry and Psychotherapy, University Medicine Greifswald, Greifswald, Germany
572) Institute of Human Genetics, University Hospital Essen, University Duisburg-Essen, Essen, Germany
573) INSERM, U 1127, CNRS UMR 7225, Sorbonne Universités, UPMC Univ Paris 06 UMR S 1127, Paris, France
574) IGBMC, CNRS UMR 7104/INSERM U964/Université de Strasbourg, Illkirch, France
575) Vanderbilt University Medical Center, Nashville, TN, USA
576) Clinical Research, Grupo Médico Carracci, Mexico City, Mexico
577) Escuela de Ciencias de la Salud, Universidad Pontificia Bolivariana, Medellín, Colombia
578) Laboratorio de Genética Molecular, SIU, Universidad de Antioquia, Medellín, Colombia
579) School of Nursing, Louisiana State University Health Sciences Center, New Orleans, LA, USA
580) Brain Center Rudolf Magnus, University Medical Center Utrecht, Utrecht, The Netherlands
581) School of Biomedical Sciences and Pharmacy, The University of Newcastle, Callaghan, Australia
582) Priority Research Centre for Brain and Mental Health Research, Hunter Medical Research Institute, Newcastle, Australia
583) Schizophrenia Research Institute, Sydney, Australia
584) Institute of Mental Health, Singapore, Singapore
585) Assistance Publique - Hopitaux de Paris, GH Pitié-Salpêtrière, Paris, France
586) Sorbonne Université, CNRS UMR 7222 Institut des Systèmes Intelligents et Robotiques, Paris, France
587) Departments of Medicine and Psychiatry, School of Medicine University of Cantabria-IDIVAL, University Hospital Marqués de Valdecilla, Santander, Spain
588) Minerva Neurosciences Inc., Waltham, MA, USA
589) Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel
590) VA Boston Healthcare System, Boston, MA, USA
591) APC Microbiome Ireland, University College Cork, Cork, Ireland
592) Department of Psychiatry, University College Cork, Cork, Ireland
593) Neuroimaging, Cognition and Genomics (NICOG) Centre, School of Psychology, National University of Ireland Galway, Galway, Ireland
594) Center for Psychiatric Genetics, NorthShore University HealthSystem Research Institute, Evanston, IL, USA
595) Department of Psychiatry and Behavioral Neuroscience, University of Chicago, Chicago, IL, USA
596) Arkin, Amsterdam, the Netherlands
597) Department for Congenital Disorders, Statens Serum Institut, Copenhagen, Denmark
598) Department of Medical Genetics, Medical University, Sofia, Bulgaria
599) Department of Molecular Bases of Human Genetics, Institute of Molecular Genetics, Russian Academy of Sciences, Moscow, Russia
600) Latvian Biomedical Research and Study Centre, Riga, Latvia
601) Vilnius University, Vilnius, Lithuania
602) Institute of Mental Health, Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, Singapore
603) Department of Human Genetics, Institute of Molecular Genetics, Russian Academy of Sciences, Moscow, Russia
604) Hunter New England Local Health District, Newcastle, Australia
605) Department of Psychiatry, University of Helsinki, Helsinki, Finland
606) Department of Psychiatry, Psychosomatics and Psychotherapy, Center of Mental Health, University Hospital Wuerzburg, Wuerzburg, Germany
607) Department of Biomedicine, Aarhus University, Aarhus, Denmark
608) Department of Clinical Neuroscience, Centre for Psychiatry Research, Karolinska Institutet, Stockholm, Sweden
609) Centre for Neuroimaging and Cognitive Genomics (NICOG), National University of Ireland, Galway, Galway, Ireland
610) NCBES Galway Neuroscience Centre, National University of Ireland, Galway, Galway, Ireland
611) Department of Psychiatry, Royal College of Surgeons in Ireland, Dublin, Ireland
612) Department of Psychiatry and Psychotherapy, Philipps University of Marburg and Marburg University Hospital, Marburg, Germany
613) Department of Psychiatry and Psychotherapy, Jena University Hospital, Jena, Germany
614) Maastricht University Medical Centre, Maastricht, the Netherlands
615) Department of Psychosis Studies, Institute of Psychiatry, King's College London, London, United Kingdom

616) Melbourne Neuropsychiatry Centre, Department of Psychiatry, University of Melbourne & Melbourne Health, Victoria, Australia
617) Centre for Neural Engineering, Department of Electrical and Electronic Engineering, University of Melbourne, Victoria, Australia
618) Oxford Health NHS Foundation Trust, Oxford, United Kingdom
619) Department of Psychiatry, University of Oxford, Oxford, UK
620) Department of Psychiatry and Behavioral Sciences, NorthShore University HealthSystem Research Institute, Evanston, IL, USA
621) Faculty of Science, Medicine and Health, University of Wollongong, Wollongong, Australia
622) Institute of Mental Health, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
623) Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, Singapore
624) School of Biomedical Sciences, Chinese University of Hong Kong, Shatin, Hong Kong
625) KIZ-CUHK Joint Laboratory of Bioresources and Molecular Research of Common Diseases, Kunming Institute of Zoology, Chinese Academy of Sciences, Kunming, China
626) Chinese University of Hong Kong, Hong Kong
627) Bulgarian Academy of Sciences, Sofia, Bulgaria
628) Departments of Psychiatry and Genetics, Washington University School of Medicine, St. Louis, MO, USA
629) Institute of Genetics, University College London, London, UK
630) Centre for Psychiatry, Barts and the London School of Medicine and Dentistry, London, UK
631) School of Medicine & Public Health, University of Newcastle, Callaghan, Australia
632) Priority Research Centre for Health Behaviour, University of Newcastle, Callaghan, Australia
633) Research Unit, Sørlandet Hospital, Kristiansand, Norway
634) Department of Statistics and Applied Probability, University of California, Santa Barbara, CA, USA
635) Computational Research Division, Lawrence Berkeley National Laboratory, University of California at Berkeley, Berkeley, CA, USA
636) NSW Health Pathology, Newcastle, Australia
637) Virginia Institute for Psychiatric and Behavioral Genetics, Department of Psychiatry, Virginia Commonwealth University, Richmond, VA, USA
638) Institute of Psychiatry, Psychology & Neuroscience, Social Genetics & Developmental Psychiatry Center, MRC, Kings College London, London, UK
639) NIHR, Biomed Research Center for Mental Health, South London & Maudsley NHS Trust & Institute Psychiatry, London, UK
640) Departments of Psychiatry and Nutrition, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
641) Departments of Psychiatry and of Neuroscience and Physiology, SUNY Upstate Medical University, Syracuse, NY, USA
642) Department of Psychiatry, Virginia Commonwealth University, Richmond, VA, USA
643) Division Biomedical Genetics, University Medical Center Utrecht, Utrecht, the Netherlands
644) Department of Psychiatry and UF Genetics Institute, University of Florida, Gainesville, FL, USA
645) Division of Cognitive and Behavioral Neurology, Brigham and Women's Hospital, Boston, MA, USA
646) Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, University College London, London, UK
647) Department of Neurology, Yale School of Medicine, New Haven, CT, USA
648) Department of Genetics and Psychiatry, University of North Carolina School of Medicine, Chapel Hill, North Carolina, USA
649) Neuropsychiatric Genetics Research Group, Department of Psychiatry, Trinity College Dublin, Ireland

† These authors jointly supervised this work
*[1] verneri.anttila@gmail.com
*[2] acorvin@tcd.ie
*[3] bneale@broadinstitute.org

One Sentence Summary: Comprehensive heritability analysis of brain phenotypes demonstrates a clear role for common genetic variation across neurological and psychiatric disorders and behavioral-cognitive traits, with substantial overlaps in genetic risk.

Abstract: Disorders of the brain can exhibit considerable epidemiological comorbidity and share symptoms, provoking debate about their etiologic overlap. We quantified the genetic sharing of 25 brain disorders from genome-wide association studies of 215,683 patients and 657,164 controls, and their relationship to 17 phenotypes from 1,191,588 individuals. Psychiatric disorders share common variant risk, while neurological disorders appear more distinct from one another and from the psychiatric disorders. We also identify significant sharing between disorders and a number of brain phenotypes, including cognitive measures. Simulations were used to explore how power, diagnostic misclassification and phenotypic heterogeneity affect genetic correlations. These results highlight the importance of common genetic

variation as a risk factor for brain disorders and the value of heritability-based methods in understanding their etiology.

Main Text:

The classification of brain disorders has evolved over the past century, reflecting the medical and scientific communities' assessments of the presumed root causes of clinical phenomena such as behavioral change, loss of motor function, spontaneous movements or alterations of consciousness. Directly observable phenomena (such as the presence of emboli, protein tangles, or unusual electrical activity patterns) generally define and separate neurological disorders from psychiatric disorders(*1*). Understanding the genetic underpinnings and categorical distinctions between brain disorders may be helpful in informing the search for the biological pathways underlying their pathophysiology(*2, 3*).

In general, brain disorders (excepting those caused by trauma, infection, or cancer) show substantial heritability from twin and family studies(*4*). Epidemiological and twin studies have explored patterns of phenotypic overlaps(*5-7*), and comorbidity has been reported for many pairs of disorders, including bipolar disorder-migraine(*8*), stroke-major depressive disorder(MDD)(*9*), epilepsy-autism spectrum disorders (ASD), and epilepsy-attention deficit hyperactivity disorder (ADHD)(*10, 11*). Furthermore, there may also be direct etiological links, as e.g. mutations in the same ion channel genes confer pleiotropic risk for multiple distinct brain phenotypes(*12-14*). Genome-wide association studies (GWAS) have demonstrated that individual common risk variants can overlap across traditional diagnostic boundaries(*15, 16*), and that disorders like schizophrenia, MDD, and bipolar disorder can have genetic correlations(*17*).

GWAS have also demonstrated that common genetic variation contributes to the heritability of brain disorders. Generally, this occurs via the combination of many common variants, each with a small individual effect, with examples in Alzheimer's disease(*18*), bipolar disorder(*19*), migraine(*20*), Parkinson's disease(*21*), and schizophrenia(*22*). In addition to locus discovery, the degree of distinctiveness(*23*) across neurological and psychiatric phenotypes can be evaluated with the introduction of novel heritability-based methods(*24*) and sufficiently large sample sizes for robust heritability analysis. These analyses can shed light on the nature of these diagnostic boundaries and explore the extent of shared common variant genetic influences.

Study design

The Brainstorm consortium is a collaboration among GWAS meta-analysis consortia of 25 disorders (see Table 1), to perform a comprehensive heritability and correlation analysis of brain disorders. We included meta-analyses of any common brain disorders for which we could identify a GWAS meta-analysis consortium of sufficient size for heritability analysis. The total study sample consists of 215,683 cases of different brain disorders and 657,164 controls (Table 1), and

includes at least one representative of most ICD-10 blocks covering mental and behavioral disorders and diseases of the central nervous system. Also included are 1,191,588 samples for 13 "behavioral-cognitive" phenotypes (n=744,486) traditionally viewed as brain-related, and four "additional" phenotypes (n=447,102) selected to represent known, well-delineated etiological processes (immune disorders [Crohn's disease], vascular disease [coronary artery disease] and anthropomorphic measures [height and BMI]; Table 2).

GWAS summary statistics for the 42 disorders and phenotypes were centralized and underwent uniform quality control and processing(*25*)*(83)*. We used European-only meta-analyses for each disorder to avoid potential bias arising from ancestry differences, generating new meta-analyses for those datasets where the original sample sets had diverse ancestries. Clinically relevant subtypes from three disorders (epilepsy, migraine, and ischemic stroke) were also included; in these cases, the subtype datasets are parts of the top-level dataset (Table 1).

We have developed a heritability estimation method, linkage disequilibrium score regression (LDSC)(*24*), which was used to calculate heritability estimates and correlations, as well as to estimate their statistical significance from block jack-knife-based standard errors. More formally, we estimate the common variant heritability (h^2g) of each disorder, defined as the proportion of phenotypic variance in the population that could theoretically be explained by an optimal linear predictor formed using the additive effects of all common (minor allele frequency > 5%) autosomal SNPs. The genetic correlation for a pair of phenotypes is then defined as the correlation between their optimal genetic predictors. Heritability for binary disorders and phenotypes was transformed to the liability scale. We further performed a weighted-least squares regression analysis to evaluate whether differences relating to study makeup (such as sample size) were correlated with the magnitude of the correlation estimates. Finally, we performed a heritability partitioning analysis*(83)* using stratified LD score regression to examine whether the observed heritability for the disorders or phenotypes was enriched into any of the tissue-specific regulatory regions or functional category partitions of the genome, using ten top-level tissue-type and 53 functional partitions from Finucane et al.(*26*). Finally, simulated phenotype data was generated under different scenarios by permuting 120,267 genotyped individuals from the UK Biobank(*25*) to evaluate power and aid in interpreting the results(*83*).

Heritability estimates and their error sources

We observed a similar range of heritability estimates among the disorders and the behavioral-cognitive phenotypes (Fig. S1A-B and Table S1, S2), roughly in line with previously reported estimates from smaller datasets (Table S3). Three ischemic stroke subtypes (cardioembolic, large-vessel disease, and small-vessel disease) as well as the "agreeableness" personality measure from NEO Five-Factor Inventory(*27*) had insufficient evidence of additive heritability for robust analysis and thus were excluded from further analysis(*25*). The only

observed correlation between heritability estimates and factors relating to study makeup (Table S4; Fig. S1C-F) was a modest correlation between age of onset of the disorder and heritability, suggesting that early-onset brain disorders tend to be more heritable. Since some of our interpretation of the results depends on lack of observed correlation, we explored the behavior of observed correlation versus power (Fig. S2A), standard errors (Fig. S2B) and the individual results (Fig. S2C and D) to identify where we can be reasonably robust in claiming lack of correlation.

The common variant heritability estimates for the psychiatric and neurological disorders were generally somewhat lower than previously reported estimates from common variants (Table S5). A similar pattern was observed for the behavioral-cognitive traits, when comparing estimates reported here with those previously reported in smaller sample sizes(*28*) with the exception of 'openness', 'neuroticism', and 'never/ever smoked', suggesting that some attenuation in heritability is observed when moving to larger sample sizes. Measures related to cognitive ability, such as childhood cognitive performance (heritability estimate of 0.19, [SE 0.03]) and years of education (heritability estimate of 0.30 [SE 0.01]), yielded estimates that were more consistent with previous estimates of the heritability of intelligence(*29, 30*), suggesting that the cognitive measures may be less prone to phenotypic measurement error and/or have a higher heritability overall than the personality measures.

These heritability estimates should be interpreted somewhat cautiously, as they reflect the phenotype ascertained in each study, and will be deflated in the presence of diagnostic heterogeneity, ascertainment errors or unusual contributions of high-impact rare variants. To evaluate potential sources of these differences, we explored three approaches*(83)*: evaluating the differences in real data, simulation work (Table S5), and quantifying the magnitude of effect for potentially implied misclassification (Table S6).

In comparison to heritability estimates obtained using twin and family data, the more diverse selection and survival biases in the underlying data may attenuate the heritability estimates and correlations, as might increased within-disorder heterogeneity introduced by the larger meta-analyses. A related explanation for the lower estimates of heritability may be that increasing sample sizes have led to expanded inclusion criteria, meaning that less severely affected cases with a lower overall burden of risk factors (both genetic and environmental) might be included, which in turn would attenuate estimates of heritability. However, the successful identification of genome-wide significant loci suggests that these larger samples are nevertheless very useful for genetic studies, and the simulation results suggest that this has at most a limited effect on estimated genetic correlations (Fig S9). Even so, some of the pairs of phenotypes included here lack sufficient power for robust estimation of genetic correlations. Moreover, our analyses only examine the properties of common variant contributions and extending these analyses to include the effects of rare variants may further inform the extent of genetic overlap. For example, epilepsy and ASD show substantial overlap in genetic risk from de novo loss of functional mutations(*31*), in contrast to the limited common variant sharing observed in this study. This may suggest that the rare and common

variant contributions to genetic overlap may behave differently and that incorporating the two variant classes into a single analysis may provide further insight into brain disorder pathogenesis.

To address the possibility of methodological differences contributing to the differences in the estimates and although LDSC and REML have previously been shown to yield similar estimates from the same data(*24*), we performed our own comparison in Alzheimer's disease(*32*) (selected based on data availability). In Alzheimer's disease, the previously published heritability estimate (0.24 [SE 0.03]) is significantly different from the estimate in the current study (0.13 [SE 0.02]). These differences may reflect implicit heterogeneity in a much larger case collection used in the current study (effective sample size 10,494 vs. 46,669) and the potential reasons listed above, but they could also be due to methodological variability (most of the previous estimated listed in Table S3 are estimated with a different methodology). To evaluate this, we applied the same analytical process used in this paper to the summary statistics of the GERAD cohort (3,941 cases and 7,848 controls) from the Alzheimer's disease meta-analysis, where the previous heritability estimate was calculated. There, we obtained a heritability estimate of 0.25 [SE 0.04], which agrees closely with the published estimate of 0.24 [SE 0.03], suggesting that the different estimates may reflect differences between datasets rather than methodological variability.

Correlations among brain disorders

We observed widespread sharing across psychiatric disorders (Fig. 1 and S3) by expanding the number of brain disorder pairs studied beyond those previously reported(*17*), but similar sharing was not observed among neurological disorders. Among the psychiatric disorders, schizophrenia showed significant genetic correlation with most of the psychiatric disorders, while MDD was positively (though not necessarily significantly) correlated with every other disorder tested. Further, schizophrenia, bipolar disorder, anxiety disorders, MDD, and ADHD each showed a high degree of correlation to the four others (average genetic correlation [r_g]=0.40; Table S7A). Anorexia nervosa, obsessive-compulsive disorder (OCD), and schizophrenia also demonstrated significant sharing amongst themselves (Fig. 1). However, the common variant risk of both ASD and Tourette Syndrome (TS) appear to be distinct from other psychiatric disorders, although with significant correlation between TS, OCD, and MDD, as well as between ASD and schizophrenia. Similarly, post-traumatic stress disorder (PTSD) showed no significant correlation with any of the other psychiatric phenotypes (though some correlation to ADHD and MDD was observed). The modest power of the ASD, PTSD, and TS meta-analyses, however, limits the strength of this conclusion (Fig. S2C).

Neurological disorders showed a more limited extent of genetic correlation than the psychiatric disorders (Fig. 2 and S4, Table S7A), suggesting greater diagnostic specificity and/or more distinct etiologies. Parkinson's disease, Alzheimer's disease, generalized epilepsy, and multiple sclerosis showed little to no correlation with other brain disorders. The highest degree of

genetic correlation among the neurological disorders was observed with focal epilepsy (average r_g =0.46, excluding the other epilepsy datasets), though none were significant, reflecting the relatively modest power of the current focal epilepsy meta-analysis (Fig. S2C). However, the modest heritability and the broad pattern of sharing observed for focal epilepsy may be consistent with heterogeneity and potentially even diagnostic misclassification across a range of neurological conditions.

In the cross-category correlation analysis, the observed pattern is consistent with limited sharing across the included neurological and psychiatric disorders (Fig. 3; average r_g=0.03). The only significant cross-category correlations were with migraine, suggesting it may share some of its genetic architecture with psychiatric disorders; migraine-ADHD (r_g=0.26, p=8.81 x 10^{-8}), migraine-TS (r_g=0.19, p=1.80 x 10^{-5}), and migraine-MDD (r_g=0.32, p=1.42 x 10^{-22} for all migraine, r_g=0.23, p=5.23 x 10^{-5} for migraine without aura, r_g=0.28, p=1.00 x 10^{-4} for migraine with aura).

We observed several significant genetic correlations between the behavioral-cognitive or additional phenotypes and brain disorders (Fig. 4 and Table S7B). Results for cognitive traits were dichotomous among psychiatric phenotypes (Fig. S5A), with ADHD, anxiety disorders, MDD, and TS showing negative correlations to the cognitive measures and anorexia nervosa, ASD, bipolar disorder and OCD showing positive correlations. Schizophrenia showed more mixed results, with significantly negative correlation to intelligence but positive correlation to years of education. Among neurological phenotypes (Fig. S5B), the correlations were either negative or null, with Alzheimer's disease, epilepsy, ICH, ischemic stroke, early-onset stroke, and migraine showing significantly negative correlations. Correlations between college attainment and years of education with bipolar disorder(*24*), Alzheimer's disease, and schizophrenia have been previously reported(*33*)).

Among the personality and symptom measures, significant positive correlations were observed between neuroticism and anorexia nervosa, anxiety disorders, migraine, migraine without aura, MDD, OCD, schizophrenia, and TS (Fig. S6A and S6B; replicating previously reported correlations with MDD and schizophrenia(34)); between depressive symptoms and ADHD, anxiety disorder, bipolar disorder, MDD, and schizophrenia; and between subjective well-being and anxiety disorder, bipolar disorder, and MDD. For smoking-related measures, the only significant genetic correlations were between never/ever smoked and MDD (r_g=0.33, p=3.10 x 10^{-11}) as well as ADHD (r_g=0.37, p=3.15 x 10^{-6}).

Among the additional phenotypes, the two examples of disorders with well-defined etiologies had different results. Crohn's disease, representing immunological pathophysiology, showed no correlation with any of the study phenotypes, while the phenotype representing vascular pathophysiology (coronary artery disease) showed significant correlation to MDD (r_g=0.19, p=8.71 x 10^{-5}) as well as the two stroke-related phenotypes (r_g=0.69, p=2.47 x 10^{-6} to ischemic stroke and r_g=0.86, p=2.26 x 10^{-5} to early-onset stroke), suggesting shared genetic effects across

these phenotypes. Significant correlations were also observed for BMI, which was positively correlated with ADHD and MDD, and negatively correlated with anorexia nervosa (as previously reported with a different dataset(*24*)) and schizophrenia.

Our enrichment analysis (Fig. S7, Tables S8-12) demonstrated significant heritability enrichments between central nervous system (CNS) and generalized epilepsy, MDD, TS, college attainment, intelligence, neuroticism, never/ever smoked); depressive symptoms and adrenal/pancreatic cells and tissues, as well as between hematopoetic cells (category which includes immune system cells) and multiple sclerosis (Figs. S7A and S7B, Tables S8 and S9). We replicate the reported (CNS) enrichment for schizophrenia, bipolar disorder, and years of education (Tables S8, S9), and observe the reported enrichments for BMI (CNS), years of education (CNS), height (connective tissues and bone, cardiovascular system and other), and Crohn's disease (hematopoietic cells) from the same datasets (Fig. S7C, D)(*26*). We further note that the psychiatric disorders with large numbers of identified GWAS loci (bipolar disorder, MDD, and schizophrenia) and migraine, which was the only cross-correlated neurological disorder, show enrichment to conserved regions (Tables S10 and S12), while the other neurological disorders with similar numbers of loci (MS, Alzheimer's, and Parkinson's diseases) do not (Fig. S7A, B). Enrichment to conserved regions was also observed to neuroticism, intelligence and college attainment and to H3K9ac peaks for BMI (Tables S11 and S12).

Discussion

By integrating and analyzing the genome-wide association summary statistic data from consortia of 25 brain disorders, we find that psychiatric disorders broadly share a considerable portion of their common variant genetic risk, especially across schizophrenia, MDD, bipolar disorder, anxiety disorder, and ADHD, while neurological disorders are more genetically distinct. Across categories, psychiatric and neurologic disorders share relatively little common genetic risk, suggesting that multiple different and largely independently regulated etiological pathways may give rise to similar clinical manifestations (e.g., psychosis, which manifests in both schizophrenia(*35*) and Alzheimer's disease(*36*)). Except for migraine, which appears to share some genetic architecture with psychiatric disorders, the existing clinical delineation between neurology and psychiatry is corroborated at the level of common variant risk for the studied disorders.

We performed some exploratory analyses based on the observed results to address concerns about diagnostic overlap and misclassification, which are particularly relevant to psychiatric disorders due to their spectral nature. Given that the broad and continuous nature of psychiatric disorder spectra has long been clinically recognized(*37-39*) and that patients can, in small numbers, progress from one diagnosis to another(*40*), we evaluated to what extent this kind of diagnostic overlap could explain the observed correlations. Genetic correlation could arise if, for example,

patients progress through multiple diagnoses over their lifetime, or if some specific diagnostic boundaries between phenotype pairs are particularly porous to misclassification (Table S5). While it would *a priori* appear unlikely to observe large-scale misclassification of migraine as schizophrenia, for example, there may be more substantial misclassification between particular psychiatric disorders, consistent with the clinical controversies in classification. Previous work(*41*) suggests that substantial misclassification (on the order of 15-30%, depending on whether it is uni- or bi-directional) is required to introduce false levels of genetic correlation. We found that the observed levels of correlation are unlikely to appear in the absence of underlying genetic correlation (Table S6), as it is apparent that a very high degree of misclassification (up to 79%) would be required to produce the observed correlations in the absence of any true genetic correlation, and that reasonably expected misclassification would have limited impact on the observed r_g (Fig. S8). Therefore, these results suggest true sharing of a substantial fraction of the common variant genetic architecture among psychiatric disorders as well as between behavioral-cognitive measures and brain disorders. We also performed large-scale simulations to explore the effect of sample size, polygenicity and degree of correlation on power to detect significant correlations. First, we established that the observed heritability of the simulated misclassified traits in the UK Biobank data behaves as would be theoretically expected (Fig. S9A), and that the effects on observed correlation (Fig. S9B and S9C) are in line with the estimates from family data(*41*). Reasonably low levels of misclassification or changes to the exact level of heritability appear unlikely to induce significant correlations, as observed in the power analysis (Fig. S10), though a lower observed heritability caused by substantial misclassification (Fig. S9A) will decrease the power to estimate true genetic overlap.

The high degree of genetic correlation among the psychiatric disorders adds further evidence that current clinical diagnostics do not reflect specific genetic etiology for these disorders, and that genetic risk factors for psychiatric disorders do not respect clinical diagnostic boundaries. Rather, this suggests a more interconnected genetic etiology, in contrast to neurological disorders, and underscores the need to refine psychiatric diagnostics. This study may provide important 'scaffolding' to support a framework for investigating mental disorders, incorporating many levels of information to understand basic dimensions of brain function.

The observed positive genetic correlations are consistent with a few hypothetical scenarios. For example, it may reflect the existence of some portion of common genetic risk factors conferring risks for multiple psychiatric disorders and where other distinct additional factors, both genetic and non-genetic, contribute to the eventual clinical presentation. The presence of significant genetic correlation may also reflect the phenotypic overlap between any two disorders; for example, the sharing between schizophrenia and ADHD might reflect underlying difficulties in executive functioning, which are well-established in both disorders(*42*), and that the shared risk arises from a partial capture of its shared genetic component. Similarly, we might speculate that a shared mechanism underlying cognitive biases may extend from overvalued ideas to delusions (ranging from anorexia nervosa and OCD to schizophrenia), and that this heritable intermediate

trait confers pleiotropic risk to multiple outcomes. This kind of latent variable could give rise to the observed genetic correlation between disorders due to the shared portion of variation affecting that variable. While a combination of these is likely, more genome-wide significant loci are needed to evaluate these overlaps at the locus level.

Conversely, the low correlations observed across neurological disorders suggest that the current classification reflects relatively specific genetic etiologies, although the limited sample size for some of these disorders and lack of inclusion of disorders conceived as "circuit-based" in the literature, such as restless legs syndrome, sleep disorders and possibly essential tremor, constrains the full generalizability of this conclusion. Degenerative disorders (such as Alzheimer's and Parkinson's diseases) would not be expected *a priori* to share their polygenic risk profiles with a neuro-immunological disorder (like multiple sclerosis) or neurovascular disorder (like ischemic stroke). Similarly, we see limited evidence for the reported co-morbidity between migraine with aura and ischemic stroke(*43*) (r_g=0.29, p=0.099); however, the standard errors of this comparison are too high to draw strong conclusions. At the disorder subtype level, migraine with and without aura (r_g=0.48, p=1.79 x 10^{-5}) shows substantial genetic correlation, while focal and generalized epilepsy (r_g=0.16, p=0.388) show much less.

The few significant correlations across neurology and psychiatry, namely between migraine and ADHD, MDD, and TS, suggest modest shared etiological overlap across the neurology/psychiatry distinction. The co-morbidity of migraine with MDD, TS and ADHD has been previously reported in epidemiological studies(*44-47*), while in contrast, the previously reported co-morbidity between migraine and bipolar disorder seen in epidemiological studies (*48*) was not reflected in our estimate of genetic correlation (r_g=-0.03, p=0.406).

Several phenotypes show only very low-level correlations with any of the other disorders and phenotypes studied here, despite large sample size and robust evidence for heritability, suggesting their common variant genetic risk may largely be unique. Alzheimer's disease, Parkinson's disease, and multiple sclerosis show extremely limited sharing with the other phenotypes and with each other. Neuroinflammation has been implicated in the pathophysiology of each of these conditions(*49-51*), as it has for migraine(*52*) and many psychiatric conditions, including schizophrenia(*53*), but no considerable shared heritability was observed with either of those conditions nor with Crohn's disease, nor did we observe enrichment for immune-related tissues in the functional partitioning (Fig. S7) as for Crohn's disease. While this does not preclude the sharing of individual neuroinflammatory mechanisms in these disorders, the large-scale lack of shared common variant genetic influences supports the distinctiveness of disorder etiology. Further, we only observed significant enrichment of heritability for immunological cells and tissues in multiple sclerosis, showing that inflammation-specific regulatory marks in the genome do not show overall enrichment for common variant risk for either Alzheimer's or Parkinson's diseases (though this does not preclude the effects of specific, non-polygenic neuroinflammatory mechanisms(*54*)). Among psychiatric disorders, ASD and TS showed a similar absence of correlation with other disorders, although this could reflect small sample sizes.

Analysis of the Big Five personality measures suggest that the current sample sizes may be large enough for correlation testing; neuroticism, which has by far the largest sample size, shows several significant correlations. Most significant of these was to MDD (r_g=0.737, p=5.04 x 10^{-96}), providing evidence for the link between these phenotypes, as reported for polygenic risk scores(*55*) and twin studies(*56, 57*); as well as other psychiatric disorders (Fig. 4, Table S7B). The correlation between MDD and anxiety disorders, with a similar pattern of correlation and the dimensional measures of depressive symptoms, subjective well-being, and neuroticism suggests that they all tag a similar underlying etiology. The significant correlation between coronary artery disease and MDD supports the link between MDD and CAD(*58*), while the observed correlation between ADHD and smoking initiation (r_g=0.374, p=3.15 x 10^{-6}) is consistent with the epidemiological evidence of overlap(*59*) and findings from twin studies(*60*).

For the neurological disorders, five (Alzheimer's disease, intracerebral hemorrhage, ischemic and early-onset stroke, and migraine) showed significant negative genetic correlation to the cognitive measures, while a two (epilepsy and focal epilepsy) showed moderate negative genetic correlation (Fig. S5). For Alzheimer's disease, poor cognitive performance in early life has been linked to increased risk for developing the disorder(*61*), but to our knowledge no such connection has been reported for other phenotypes. Among the psychiatric disorders, ADHD, anxiety disorders and MDD show a significant negative correlation to cognitive and education attainment measures, while the remaining five of the eight psychiatric disorders (anorexia nervosa, ASD, bipolar disorder, OCD, and schizophrenia) showed significant positive genetic correlation with one or more cognitive measures. These results suggest the existence of a link between cognitive performance in early life and the genetic risk for both psychiatric and neurological brain disorders. The basis of the genetic correlations between education, cognition and brain disorders may have a variety of root causes including indexing performance differences on the basis of behavioral dysregulation (e.g., ADHD relating to attentional problems during cognitive tests) or may reflect ascertainment biases in certain disorders conditional on impaired cognition (e.g., individuals with lower cognitive reserve being more rapidly identified for Alzheimer's disease), but the results could also suggest a direct link between the underlying etiologies.

BMI shows significant positive genetic correlation to ADHD, consistent with a meta-analysis linking ADHD to obesity(*62*), and negative genetic correlation with anorexia nervosa, OCD, and schizophrenia. This is consistent with evidence for enrichment of BMI heritability in CNS tissues(*26*) that suggest neuronal involvement(*63*); this may also provide a partial genetic explanation for lower BMI in anorexia nervosa patients even after recovery(*64*). Given that no strong correlations were observed between BMI and any of the neurological phenotypes, it may be that BMI's brain-specific genetic architecture is more closely related to behavioral phenotypes. Ischemic stroke and BMI show surprisingly little genetic correlation in this analysis (r_g=0.07, p=0.26), suggesting that although BMI is a risk factor for stroke(*65*), there is little evidence for shared common genetic effects. These analyses also suggest that the reported reduced rates of cardiovascular disease in individuals with histories of anorexia nervosa(*66, 67*) are more likely

due to BMI-related secondary effects. The limited evidence of genetic correlation of anorexia nervosa with intracerebral hemorrhage, ischemic stroke, early-onset stroke and coronary artery disease suggest that any lower cardiovascular mortality is more likely due to direct BMI-related effects rather than genetic risk variants.

The genetic correlation results presented here indicate that the clinical boundaries for the studied psychiatric phenotypes do not reflect distinct underlying pathogenic processes. This suggests that genetically informed analyses may provide a basis for restructuring of psychiatric nosology, consistent with twin and family-based results. In contrast, neurological disorders show greater genetic specificity, and although it is important to emphasize that while some brain disorders are under-represented here, our results demonstrate the limited evidence for widespread common genetic risk sharing between psychiatric and neurological disorders. However, we provide strong evidence that both psychiatric and neurological disorders show robust correlations with cognitive and personality measures, suggesting new avenues for follow-up studies. Further study is needed to evaluate whether overlapping genetic contributions to psychiatric pathology may influence treatment choices. Ultimately, such developments give hope to reducing diagnostic heterogeneity and eventually improving the diagnostics and treatment of psychiatric disorders.

Materials and Methods

We collected GWAS meta-analysis summary statistics for 25 brain disorders and 17 other phenotypes from various consortia, and where necessary generated new, non-sex-stratified European-cohorts-only versions of the meta-analyses(*25*). All datasets underwent uniform quality control *(83).* For each trait, using the linkage disequilibrium score (LDSC) framework(*24*), the total additive common SNP heritability present in the summary statistics (h^2g) was estimated by regressing the association χ^2 statistic of a SNP against the total amount of common genetic variation tagged by that SNP, for all SNPs. Genetic correlations (r_g; i.e., the genome-wide average shared genetic risk) for pairs of phenotypes were estimated by regressing the product of Z-score for each phenotype and for each SNP, instead of the χ^2 statistic. Significance was assessed by Bonferroni multiple testing correction via estimating the number of independent brain disorder phenotypes via matrix decomposition *(83).* Functional and partitioning analyses for the GWAS datasets were also performed using LDSC. Power analyses and simulation work to aid in interpretation of the results were conducted using genotype data from the UK Biobank Resource *(83).*

Author Information Correspondence and requests for materials should be addressed to V.A. (verneri.anttila@gmail.com), A.C. (acorvin@tcd.ie), or B.M.N. (bneale@broadinstitute.org).

References:

1. J. B. Martin, The integration of neurology, psychiatry, and neuroscience in the 21st century. *Am J Psychiatry* **159**, 695-704 (2002).
2. J. W. Smoller, Disorders and borders: psychiatric genetics and nosology. *Am J Med Genet B Neuropsychiatr Genet* **162B**, 559-578 (2013).
3. T. R. Insel, P. S. Wang, Rethinking mental illness. *JAMA* **303**, 1970-1971 (2010).
4. T. J. Polderman *et al.*, Meta-analysis of the heritability of human traits based on fifty years of twin studies. *Nat Genet* **47**, 702-709 (2015).
5. K. S. Kendler, C. A. Prescott, J. Myers, M. C. Neale, The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. *Arch Gen Psychiatry* **60**, 929-937 (2003).
6. R. Jensen, L. J. Stovner, Epidemiology and comorbidity of headache. *Lancet neurology* **7**, 354-361 (2008).
7. J. Nuyen *et al.*, Comorbidity was associated with neurologic and psychiatric diseases: a general practice-based controlled study. *J Clin Epidemiol* **59**, 1274-1284 (2006).
8. R. M. Hirschfeld *et al.*, Screening for bipolar disorder in the community. *The Journal of clinical psychiatry* **64**, 53-59 (2003).
9. A. Pan, Q. Sun, O. I. Okereke, K. M. Rexrode, F. B. Hu, Depression and risk of stroke morbidity and mortality: a meta-analysis and systematic review. *JAMA* **306**, 1241-1249 (2011).
10. A. Lo-Castro, P. Curatolo, Epilepsy associated with autism and attention deficit hyperactivity disorder: is there a genetic link? *Brain & development* **36**, 185-193 (2014).
11. E. N. Bertelsen, J. T. Larsen, L. Petersen, J. Christensen, S. Dalsgaard, Childhood Epilepsy, Febrile Seizures, and Subsequent Risk of ADHD. *Pediatrics* **138**, (2016).
12. C. G. de Kovel *et al.*, Recurrent microdeletions at 15q11.2 and 16p13.11 predispose to idiopathic generalized epilepsies. *Brain* **133**, 23-32 (2010).
13. T. D. Graves, M. G. Hanna, Neurological channelopathies. *Postgraduate medical journal* **81**, 20-32 (2005).
14. J. Haan, G. M. Terwindt, A. M. van den Maagdenberg, A. H. Stam, M. D. Ferrari, A review of the genetic relation between migraine and epilepsy. *Cephalalgia* **28**, 105-113 (2008).
15. S. Debette *et al.*, Common variation in PHACTR1 is associated with susceptibility to cervical artery dissection. *Nat Genet* **47**, 78-83 (2015).
16. S. M. Purcell *et al.*, Common polygenic variation contributes to risk of schizophrenia and bipolar disorder. *Nature* **460**, 748-752 (2009).
17. C. Cross-Disorder Group of the Psychiatric Genomics *et al.*, Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. *Nat Genet* **45**, 984-994 (2013).
18. J. C. Lambert *et al.*, Meta-analysis of 74,046 individuals identifies 11 new susceptibility loci for Alzheimer's disease. *Nat Genet* **45**, 1452-1458 (2013).
19. T. W. Muhleisen *et al.*, Genome-wide association study reveals two new risk loci for bipolar disorder. *Nature communications* **5**, 3339 (2014).
20. V. Anttila *et al.*, Genome-wide meta-analysis identifies new susceptibility loci for migraine. *Nat Genet* **45**, 912-917 (2013).
21. M. A. Nalls *et al.*, Large-scale meta-analysis of genome-wide association data identifies six new risk loci for Parkinson's disease. *Nat Genet* **46**, 989-993 (2014).
22. C. Schizophrenia Working Group of the Psychiatric Genomics, Biological insights from 108 schizophrenia-associated genetic loci. *Nature* **511**, 421-427 (2014).
23. N. Solovieff, C. Cotsapas, P. H. Lee, S. M. Purcell, J. W. Smoller, Pleiotropy in complex traits: challenges and strategies. *Nat Rev Genet* **14**, 483-495 (2013).

24. B. Bulik-Sullivan *et al.*, An atlas of genetic correlations across human diseases and traits. *Nat Genet* **47**, 1236-1241 (2015).
25. Materials and methods are available as supplementary materials on Science Online.
26. H. K. Finucane *et al.*, Partitioning heritability by functional annotation using genome-wide association summary statistics. *Nat Genet* **47**, 1228-+ (2015).
27. M. H. de Moor *et al.*, Meta-analysis of genome-wide association studies for personality. *Mol Psychiatry* **17**, 337-349 (2012).
28. R. A. Power, M. Pluess, Heritability estimates of the Big Five personality traits based on common genetic variants. *Translational psychiatry* **5**, e604 (2015).
29. C. M. Haworth *et al.*, The heritability of general cognitive ability increases linearly from childhood to young adulthood. *Mol Psychiatry* **15**, 1112-1120 (2010).
30. I. J. Deary *et al.*, Genetic contributions to stability and change in intelligence from childhood to old age. *Nature* **482**, 212-215 (2012).
31. S. De Rubeis *et al.*, Synaptic, transcriptional and chromatin genes disrupted in autism. *Nature* **515**, 209-215 (2014).
32. S. H. Lee *et al.*, Estimation and partitioning of polygenic variation captured by common SNPs for Alzheimer's disease, multiple sclerosis and endometriosis. *Hum Mol Genet* **22**, 832-841 (2013).
33. A. Okbay *et al.*, Genome-wide association study identifies 74 loci associated with educational attainment. *Nature* **533**, 539-542 (2016).
34. D. J. Smith *et al.*, Genome-wide analysis of over 106 000 individuals identifies 9 neuroticism-associated loci. *Mol Psychiatry* **21**, 749-757 (2016).
35. P. F. Buckley, B. J. Miller, D. S. Lehrer, D. J. Castle, Psychiatric comorbidities and schizophrenia. *Schizophrenia bulletin* **35**, 383-402 (2009).
36. C. G. Lyketsos *et al.*, Mental and behavioral disturbances in dementia: findings from the Cache County Study on Memory in Aging. *Am J Psychiatry* **157**, 708-714 (2000).
37. R. Kendell, A. Jablensky, Distinguishing between the validity and utility of psychiatric diagnoses. *Am J Psychiatry* **160**, 4-12 (2003).
38. A. S. Cristino *et al.*, Neurodevelopmental and neuropsychiatric disorders represent an interconnected molecular system. *Mol Psychiatry* **19**, 294-301 (2014).
39. D. A. Regier *et al.*, Limitations of diagnostic criteria and assessment instruments for mental disorders. Implications for research and policy. *Arch Gen Psychiatry* **55**, 109-115 (1998).
40. T. M. Laursen, E. Agerbo, C. B. Pedersen, Bipolar disorder, schizoaffective disorder, and schizophrenia overlap: a new comorbidity index. *The Journal of clinical psychiatry* **70**, 1432-1438 (2009).
41. N. R. Wray, S. H. Lee, K. S. Kendler, Impact of diagnostic misclassification on estimation of genetic correlations using genome-wide genotypes. *Eur J Hum Genet* **20**, 668-674 (2012).
42. E. G. Willcutt, A. E. Doyle, J. T. Nigg, S. V. Faraone, B. F. Pennington, Validity of the executive function theory of attention-deficit/hyperactivity disorder: a meta-analytic review. *Biol Psychiatry* **57**, 1336-1346 (2005).
43. J. T. Spector *et al.*, Migraine headache and ischemic stroke risk: an updated meta-analysis. *The American journal of medicine* **123**, 612-624 (2010).
44. O. B. Fasmer, A. Halmoy, K. J. Oedegaard, J. Haavik, Adult attention deficit hyperactivity disorder is associated with migraine headaches. *European archives of psychiatry and clinical neuroscience* **261**, 595-602 (2011).
45. N. Breslau, R. B. Lipton, W. F. Stewart, L. R. Schultz, K. M. Welch, Comorbidity of migraine and depression: investigating potential etiology and prognosis. *Neurology* **60**, 1308-1312 (2003).
46. K. R. Merikangas, J. Angst, H. Isler, Migraine and psychopathology. Results of the Zurich cohort study of young adults. *Arch Gen Psychiatry* **47**, 849-853. (1990).

47. G. Barabas, W. S. Matthews, M. Ferrari, Tourette's syndrome and migraine. *Arch Neurol* **41**, 871-872 (1984).
48. R. S. McIntyre *et al.*, The prevalence and impact of migraine headache in bipolar disorder: results from the Canadian Community Health Survey. *Headache* **46**, 973-982 (2006).
49. M. T. Heneka *et al.*, Neuroinflammation in Alzheimer's disease. *Lancet neurology* **14**, 388-405 (2015).
50. E. C. Hirsch, S. Hunot, Neuroinflammation in Parkinson's disease: a target for neuroprotection? *Lancet neurology* **8**, 382-397 (2009).
51. E. M. Frohman, M. K. Racke, C. S. Raine, Multiple sclerosis--the plaque and its pathogenesis. *N Engl J Med* **354**, 942-955 (2006).
52. C. Waeber, M. A. Moskowitz, Migraine as an inflammatory disorder. *Neurology* **64**, S9-15 (2005).
53. J. Steiner *et al.*, Increased prevalence of diverse N-methyl-D-aspartate glutamate receptor antibodies in patients with an initial diagnosis of schizophrenia: specific relevance of IgG NR1a antibodies for distinction from N-methyl-D-aspartate glutamate receptor encephalitis. *JAMA psychiatry* **70**, 271-278 (2013).
54. C. International Genomics of Alzheimer's Disease, Convergent genetic and expression data implicate immunity in Alzheimer's disease. *Alzheimer's & dementia : the journal of the Alzheimer's Association* **11**, 658-671 (2015).
55. C. Genetics of Personality *et al.*, Meta-analysis of Genome-wide Association Studies for Neuroticism, and the Polygenic Association With Major Depressive Disorder. *JAMA psychiatry* **72**, 642-650 (2015).
56. K. S. Kendler, M. Gatz, C. O. Gardner, N. L. Pedersen, Personality and major depression: a Swedish longitudinal, population-based twin study. *Arch Gen Psychiatry* **63**, 1113-1120 (2006).
57. R. E. Orstavik, K. S. Kendler, N. Czajkowski, K. Tambs, T. Reichborn-Kjennerud, The relationship between depressive personality disorder and major depressive disorder: a population-based twin study. *Am J Psychiatry* **164**, 1866-1872; quiz 1924 (2007).
58. H. Hemingway, M. Marmot, Evidence based cardiology: psychosocial factors in the aetiology and prognosis of coronary heart disease. Systematic review of prospective cohort studies. *BMJ* **318**, 1460-1467 (1999).
59. F. J. McClernon, S. H. Kollins, ADHD and smoking: from genes to brain to behavior. *Ann N Y Acad Sci* **1141**, 131-147 (2008).
60. T. Korhonen *et al.*, Externalizing behaviors and cigarette smoking as predictors for use of illicit drugs: a longitudinal study among Finnish adolescent twins. *Twin Res Hum Genet* **13**, 550-558 (2010).
61. D. A. Snowdon *et al.*, Linguistic ability in early life and cognitive function and Alzheimer's disease in late life. Findings from the Nun Study. *JAMA* **275**, 528-532 (1996).
62. S. Cortese *et al.*, Association Between ADHD and Obesity: A Systematic Review and Meta-Analysis. *Am J Psychiatry* **173**, 34-43 (2016).
63. D. Shungin *et al.*, New genetic loci link adipose and insulin biology to body fat distribution. *Nature* **518**, 187-196 (2015).
64. L. Mustelin *et al.*, Long-term outcome in anorexia nervosa in the community. *The International journal of eating disorders* **48**, 851-859 (2015).
65. T. Kurth *et al.*, Prospective study of body mass index and risk of stroke in apparently healthy women. *Circulation* **111**, 1992-1998 (2005).
66. S. R. Korndorfer *et al.*, Long-term survival of patients with anorexia nervosa: a population-based study in Rochester, Minn. *Mayo Clinic proceedings* **78**, 278-284 (2003).
67. P. F. Sullivan, Discrepant results regarding long-term survival of patients with anorexia nervosa? *Mayo Clinic proceedings* **78**, 273-274 (2003).

68. L. Duncan *et al.*, Significant Locus and Metabolic Genetic Correlations Revealed in Genome-Wide Association Study of Anorexia Nervosa. *Am J Psychiatry*, appiajp201716121402 (2017).
69. T. Otowa *et al.*, Meta-analysis of genome-wide association studies of anxiety disorders. *Mol Psychiatry* **21**, 1391-1399 (2016).
70. C. Autism Spectrum Disorders Working Group of The Psychiatric Genomics, Meta-analysis of GWAS of over 16,000 individuals with autism spectrum disorder highlights a novel locus at 10q24.32 and a significant overlap with schizophrenia. *Molecular autism* **8**, 21 (2017).
71. I. L. A. E. C. o. C. Epilepsies, Genetic determinants of common epilepsies: a meta-analysis of genome-wide association studies. *Lancet neurology* **13**, 893-903 (2014).
72. D. Woo *et al.*, Meta-analysis of genome-wide association studies identifies 1q22 as a susceptibility locus for intracerebral hemorrhage. *Am J Hum Genet* **94**, 511-521 (2014).
73. M. Traylor *et al.*, Genetic risk factors for ischaemic stroke and its subtypes (the METASTROKE collaboration): a meta-analysis of genome-wide association studies. *Lancet neurology* **11**, 951-962 (2012).
74. N. A. Patsopoulos *et al.*, Genome-wide meta-analysis identifies novel multiple sclerosis susceptibility loci. *Ann Neurol* **70**, 897-912 (2011).
75. C. A. Rietveld *et al.*, GWAS of 126,559 individuals identifies genetic variants associated with educational attainment. *Science* **340**, 1467-1471 (2013).
76. C. A. Rietveld *et al.*, Common genetic variants associated with cognitive performance identified using the proxy-phenotype method. *Proc Natl Acad Sci U S A* **111**, 13790-13794 (2014).
77. S. Sniekers *et al.*, Genome-wide association meta-analysis of 78,308 individuals identifies new loci and genes influencing human intelligence. *Nat Genet* **49**, 1107-1112 (2017).
78. A. Okbay *et al.*, Genetic variants associated with subjective well-being, depressive symptoms, and neuroticism identified through genome-wide analyses. *Nat Genet* **48**, 624-633 (2016).
79. Tobacco, C. Genetics, Genome-wide meta-analyses identify multiple loci associated with smoking behavior. *Nat Genet* **42**, 441-447 (2010).
80. A. R. Wood *et al.*, Defining the role of common variation in the genomic and biological architecture of adult human height. *Nat Genet* **46**, 1173-1186 (2014).
81. L. Jostins *et al.*, Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. *Nature* **491**, 119-124 (2012).
82. H. Schunkert *et al.*, Large-scale association analysis identifies 13 new susceptibility loci for coronary artery disease. *Nat Genet* **43**, 333-338 (2011).
83. See Supplementary Materials.

Supplementary references

84. International HapMap Consortium *et al.*, Integrating common and rare genetic variation in diverse human populations. *Nature* **467**, 52-58 (2010).
85. C. Sudlow *et al.*, UK Biobank: An open access resource for identifying the causes of a wide range of complex diseases of middle and old age. *PLoS Med* **12**, e1001779 (2015).
86. C. C. Chang *et al.*, Second-generation PLINK: rising to the challenge of larger and richer datasets. *Gigascience* **4**, 7 (2015).
87. B. Bulik-Sullivan *et al.*, An atlas of genetic correlations across human diseases and traits. *Nat Genet* **47**, 1236-1241 (2015).

88. B. K. Bulik-Sullivan *et al.*, LD Score regression distinguishes confounding from polygenicity in genome-wide association studies. *Nat Genet* **47**, 291-295 (2015).

89. W. J. Peyrot, D. I. Boomsma, B. W. Penninx, N. R. Wray, Disease and polygenic architecture: Avoid trio design and appropriately account for unscreened control subjects for common disease. *Am J Hum Genet* **98**, 382-391 (2016).

90. D. R. Nyholt, A simple correction for multiple testing for single-nucleotide polymorphisms in linkage disequilibrium with each other. *Am J Hum Genet* **74**, 765-769 (2004).

91. J. Li, L. Ji, Adjusting multiple testing in multilocus analyses using the eigenvalues of a correlation matrix. *Heredity* **95**, 221-227 (2005).

92. H. K. Finucane *et al.*, Partitioning heritability by functional annotation using genome-wide association summary statistics. *Nat Genet* **47**, 1228-1235 (2015).

93. A. Okbay *et al.*, Genetic variants associated with subjective well-being, depressive symptoms, and neuroticism identified through genome-wide analyses. *Nat Genet* **48**, 624-633 (2016).

94. L. Duncan *et al.*, Significant locus and metabolic genetic correlations revealed in genome-wide association study of anorexia nervosa. *Am J Psychiatry* **174**, 850-858 (2017).

95. T. Otowa *et al.*, Meta-analysis of genome-wide association studies of anxiety disorders. *Mol Psychiatry* **21**, 1391-1399 (2016).

96. Autism Spectrum Disorders Working Group of The Psychiatric Genomics Consortium, Meta-analysis of GWAS of over 16,000 individuals with autism spectrum disorder highlights a novel locus at 10q24.32 and a significant overlap with schizophrenia. *Mol Autism* **8**, 21 (2017).

97. L. E. Duncan *et al.*, Largest GWAS of PTSD (N=20 070) yields genetic overlap with schizophrenia and sex differences in heritability. *Mol Psychiatry* **23**, 666-673 (2018).

98. Schizophrenia Working Group of the Psychiatric Genomics Consortium, Biological insights from 108 schizophrenia-associated genetic loci. *Nature* **511**, 421-427 (2014).

99. J. C. Lambert *et al.*, Meta-analysis of 74,046 individuals identifies 11 new susceptibility loci for Alzheimer's disease. *Nat Genet* **45**, 1452-1458 (2013).

100. International League Against Epilepsy Consortium on Complex Epilepsies, Genetic determinants of common epilepsies: a meta-analysis of genome-wide association studies. *Lancet Neurol* **13**, 893-903 (2014).

101. D. Woo *et al.*, Meta-analysis of genome-wide association studies identifies 1q22 as a susceptibility locus for intracerebral hemorrhage. *Am J Hum Genet* **94**, 511-521 (2014).

102. M. Traylor *et al.*, Genetic risk factors for ischaemic stroke and its subtypes (the METASTROKE collaboration): a meta-analysis of genome-wide association studies. *Lancet Neurol* **11**, 951-962 (2012).

103. P. Gormley *et al.*, Meta-analysis of 375,000 individuals identifies 38 susceptibility loci for migraine. *Nat Genet* **48**, 856-866 (2016).

104. N. A. Patsopoulos *et al.*, Genome-wide meta-analysis identifies novel multiple sclerosis susceptibility loci. *Ann Neurol* **70**, 897-912 (2011).

105. International Parkinson Disease Genomics Consortium *et al.*, Imputation of sequence variants for identification of genetic risks for Parkinson's disease: a meta-analysis of genome-wide association studies. *Lancet* **377**, 641-649 (2011).

106. Cross-Disorder Group of the Psychiatric Genomics Consortium *et al.*, Genetic relationship between five psychiatric disorders estimated from genome-wide SNPs. *Nat Genet* **45**, 984-994 (2013).

107. J. I. Hudson, E. Hiripi, H. G. Pope, Jr., R. C. Kessler, The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. *Biol Psychiatry* **61**, 348-358 (2007).

108. V. Boraska *et al.*, A genome-wide association study of anorexia nervosa. *Mol Psychiatry* **19**, 1085-1094 (2014).

109. M. Karno, J. M. Golding, S. B. Sorenson, M. A. Burnam, The epidemiology of obsessive-compulsive disorder in five US communities. *Arch Gen Psychiatry* **45**, 1094-1099 (1988).

110. R. C. Kessler, A. Sonnega, E. Bromet, M. Hughes, C. B. Nelson, Posttraumatic stress disorder in the National Comorbidity Survey. *Arch Gen Psychiatry* **52**, 1048-1060 (1995).

111. M. M. Robertson, The prevalence and epidemiology of Gilles de la Tourette syndrome. Part 1: the epidemiological and prevalence studies. *J Psychosom Res* **65**, 461-472 (2008).

112. D. C. Hesdorffer *et al.*, Estimating risk for developing epilepsy: a population-based study in Rochester, Minnesota. *Neurology* **76**, 23-27 (2011).

113. V. L. Feigin, C. M. Lawes, D. A. Bennett, S. L. Barker-Collo, V. Parag, Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review. *Lancet Neurol* **8**, 355-369 (2009).

114. R. Bonita, N. Solomon, J. B. Broad, Prevalence of stroke and stroke-related disability. Estimates from the Auckland stroke studies. *Stroke* **28**, 1898-1902 (1997).

115. R. B. Lipton, W. F. Stewart, S. Diamond, M. L. Diamond, M. Reed, Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache* **41**, 646-657 (2001).

116. M. B. Russell, V. Ulrich, M. Gervil, J. Olesen, Migraine without aura and migraine with aura are distinct disorders. A population-based twin survey. *Headache* **42**, 332-336 (2002).

117. B. K. MacDonald, O. C. Cockerell, J. W. Sander, S. D. Shorvon, The incidence and lifetime prevalence of neurological disorders in a prospective community-based study in the UK. *Brain* **123**, 665-676 (2000).

118. A. Okbay *et al.*, Genome-wide association study identifies 74 loci associated with educational attainment. *Nature* **533**, 539-542 (2016).

119. C. A. Rietveld *et al.*, GWAS of 126,559 individuals identifies genetic variants associated with educational attainment. *Science* **340**, 1467-1471 (2013).

120. B. Benyamin *et al.*, Childhood intelligence is heritable, highly polygenic and associated with FNBP1L. *Mol Psychiatry* **19**, 253-258 (2014).

121. S. Sniekers *et al.*, Genome-wide association meta-analysis of 78,308 individuals identifies new loci and genes influencing human intelligence. *Nat Genet* **49**, 1107-1112 (2017).

122. S. M. van den Berg *et al.*, Meta-analysis of genome-wide association studies for extraversion: Findings from the Genetics of Personality Consortium. *Behav Genet* **46**, 170-182 (2016).

123. M. H. de Moor *et al.*, Meta-analysis of genome-wide association studies for personality. *Mol Psychiatry* **17**, 337-349 (2012).

124. Tobacco and Genetics Consortium, Genome-wide meta-analyses identify multiple loci associated with smoking behavior. *Nat Genet* **42**, 441-447 (2010).

125. A. E. Locke *et al.*, Genetic studies of body mass index yield new insights for obesity biology. *Nature* **518**, 197-206 (2015).

126. A. R. Wood *et al.*, Defining the role of common variation in the genomic and biological architecture of adult human height. *Nat Genet* **46**, 1173-1186 (2014).

127. H. Schunkert *et al.*, Large-scale association analysis identifies 13 new susceptibility loci for coronary artery disease. *Nat Genet* **43**, 333-338 (2011).

128. L. Jostins *et al.*, Host-microbe interactions have shaped the genetic architecture of inflammatory bowel disease. *Nature* **491**, 119-124 (2012).

129. L. K. Davis *et al.*, Partitioning the heritability of Tourette syndrome and obsessive compulsive disorder reveals differences in genetic architecture. *PLoS Genet* **9**, e1003864 (2013).

130. S. H. Lee *et al.*, Estimation and partitioning of polygenic variation captured by common SNPs for Alzheimer's disease, multiple sclerosis and endometriosis. *Hum Mol Genet* **22**, 832-841 (2013).

131. D. Speed *et al.*, Describing the genetic architecture of epilepsy through heritability analysis. *Brain* **137**, 2680-2689 (2014).

132. W. J. Devan *et al.*, Heritability estimates identify a substantial genetic contribution to risk and outcome of intracerebral hemorrhage. *Stroke* **44**, 1578-1583 (2013).

133. S. Bevan *et al.*, Genetic heritability of ischemic stroke and the contribution of previously reported candidate gene and genomewide associations. *Stroke* **43**, 3161-3167 (2012).

134. M. F. Keller *et al.*, Using genome-wide complex trait analysis to quantify 'missing heritability' in Parkinson's disease. *Hum Mol Genet* **21**, 4996-5009 (2012).

135. T. M. Laursen, E. Agerbo, C. B. Pedersen, Bipolar disorder, schizoaffective disorder, and schizophrenia overlap: a new comorbidity index. *J Clin Psychiatry* **70**, 1432-1438 (2009).

136. P. F. Buckley, B. J. Miller, D. S. Lehrer, D. J. Castle, Psychiatric comorbidities and schizophrenia. *Schizophr Bull* **35**, 383-402 (2009).

137. K. R. Merikangas *et al.*, Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. *Arch Gen Psychiatry* **64**, 543-552 (2007).

Acknowledgments We thank the members of the Neale and Daly labs for helpful discussions, and to acknowledge R. Hoskins, J. Wessman and J. Martin for their comments on the manuscript, M. Whittall for inspiration, S. Knemeyer for help with the summary figure, C. Hammond for organizational assistance, and the patients and participants of the respective consortia for their invaluable participation. Data on coronary artery disease has been contributed by CARDIoGRAMplusC4D investigators and have been downloaded from www.CARDIOGRAMPLUSC4D.ORG. matSpD is available at neurogenetics.qimrberghofer.edu.au/matSpD/. This research has been conducted using the UK Biobank Resource (application #18597). **Funding:** This work was supported by grants 1R01MH10764901 and 5U01MH09443203 as well as the Orion Farmos Research Foundation (VA) and the Fannie and John Hertz Foundation (HKF); disorder-specific funding is detailed in the Supplementary Materials ("Study-specific acknowledgments").
Author contributions: VA, AC and BMN conceived and coordinated the study; VA, BBS, HKF, RW and PT contributed methodology; BBS and HKF contributed software; VA and BMN conducted the statistical analysis; BMN obtained funding and provided resources; RW, JB, LD, VE-P, GF, PG, RM, NP, SR, ZW, and DY were responsible for curation of disorder-specific data; PHL and CC helped with data interpretation; VA and BMN wrote the original draft, and all authors contributed to review and editing; VA provided the visualization; GB, CB, MDaly, MDichgans, SVF, RG, PH, KK, BK, CAM, AP, JS, PS, JW, NW, CC, AP, JS, PS, JR, AC, BMN provided supervision and project administration; remaining authors contributed disorder-specific sample collection and/or analysis (Consortium-specific lists can be found in the Supplementary Materials). **Competing interests:** Authors report no competing interests. **Data and materials availability:** Data sources for the GWAS summary statistics used in the study and their availability, as well as the study-specific acknowledgments, are listed in Supplementary Materials (Table S13 and Supplementary text, respectively).

Figure 1. *Genetic correlations across psychiatric phenotypes.*

Color of each box indicates the magnitude of the correlation, while size of the boxes indicates its significance (LDSC), with significant correlations filling each box completely. Asterisks indicate genetic correlations which are significantly different from zero after Bonferroni correction. ADHD – attention deficit hyperactivity disorder; ASD – autism spectrum disorder; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder.

Figure 2. *Genetic correlations across neurological phenotypes.*

Color of each box indicates the magnitude of the correlation, while size of the boxes indicates its significance (LDSC), with significant correlations filling each box completely. Asterisks indicate genetic correlations which are significantly different from zero after Bonferroni correction. Some phenotypes have substantial overlaps (see Table 1), e.g. all cases of generalized epilepsy are also cases of epilepsy. Asterisks indicate significant genetic correlation after multiple testing correction. ICH – intracerebral hemorrhage.

Figure 3. *Genetic correlations across neurological and psychiatric phenotypes.*

Color of each box indicates the magnitude of the correlation, while size of the boxes indicates its significance (LDSC), with significant correlations filling each box completely. Asterisks indicate genetic correlations which are significantly different from zero after Bonferroni correction. ADHD – attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder.

Figure 4. *Genetic correlations across brain disorders and behavioral-cognitive phenotypes.*

Color of each box indicates the magnitude of the correlation, while size of the boxes indicates its significance (LDSC), with significant correlations filling each box completely. Asterisks indicate genetic correlations which are significantly different from zero after Bonferroni correction. ADHD – attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder; BMI –body-mass index.

Table 1. *Brain disorder phenotypes used in the Brainstorm project.*

Psychiatric disorders				**Neurological disorders**			
Disorder	Source	Cases	Controls	Disorder	Source	Cases	Controls
ADHD	PGC-ADD2	12,645	84,435	Alzheimer's disease	IGAP	17,008	37,154
Anorexia nervosa	PGC-ED	3,495	11,105	Epilepsy	ILAE	7,779	20,439
Anxiety disorders	ANGST	5,761	11,765	Focal epilepsy	"	4,601	17,985
Autism spectrum disorder	PGC-AUT	6,197	7,377	Generalized epilepsy	"	2,525	16,244
Bipolar disorder	PGC-BIP2	20,352	31,358	Intracerebral hemorrhage	ISGC	1,545	1,481
Major depressive disorder	PGC-MDD2	16,823	25,632	Ischemic stroke	METASTROKE	10,307	19,326
OCD	PGC-OCDTS	2,936	7,279	Cardioembolic stroke	"	1,859	17,708
PTSD	PGC-PTSD	2,424	7,113	Early-onset stroke	"	3,274	11,012
Schizophrenia	PGC-SCZ2	33,640	43,456	Large-vessel disease	"	1,817	17,708
Tourette Syndrome	PGC-OCDTS	4,220	8,994	Small-vessel disease	"	1,349	17,708
				Migraine	IHGC	59,673	316,078
				Migraine with aura	"	6,332	142,817
				Migraine without aura	"	8,348	136,758
				Multiple sclerosis	IMSGC	5,545	12,153
				Parkinson's disease	IPDGC	5,333	12,019
Total psychiatric		*108,493*	*238,514*	*Total neurologic*		*107,190*	*418,650*

Indented phenotypes are part of a larger whole, e.g. the epilepsy study contains the samples from both focal epilepsy and generalized epilepsy; sample counts for such overlaps are shown in gray. ADHD – attention deficit hyperactivity disorder; OCD – obsessive-compulsive disorder. 'Anxiety disorders' refers to a meta-analysis of five subtypes (generalized anxiety disorder, panic disorder, social phobia, agoraphobia, and specific phobias). References are listed in Table S1 and data availability in Table S13.

Table 2. *Behavioral-cognitive and additional phenotypes used in the study.*

Phenotype	Source	Samples
Behavioral-cognitive phenotypes		
Cognitive		
Years of education (q)	SSGAC	293,723
College attainment (d)	"	120,917
Cognitive performance (q)	"	17,989
Intelligence (d)	CTG	78,308
Personality measures		
Subjective well-being	SSGAC	298,420
Depressive symptoms	"	161,460
Neuroticism (q)	"	170,911
Extraversion (q)	GPC	63,030
Agreeableness (q)	"	17,375
Conscientiousness (q)	"	17,375
Openness (q)	"	17,375
Smoking-related		
Never/ever smoked (d)	TAG	74,035
Cigarettes per day (q)	TAG	38,617
Additional phenotypes		
BMI (q)	GIANT	339,224
Height (q)	"	253,288
Coronary artery disease (d)	Cardiogram	86,995
Crohn's disease (d)	IIBDGC	20,883
Total		**1,124,048**

Indented phenotypes are part of a larger whole, e.g. samples in the college attainment analysis are a subset of those in the analysis for years of education; sample counts for such overlaps are shown in gray. (d) – dichotomous phenotype, (q) – quantitative phenotype. BMI – body-mass index. References and phenotype definitions are listed in Table S2, and data availability in Table S13.

Supplementary Materials

Materials and methods

Supplementary Text

Effect of co-morbidity and phenotypic misclassification

Study-specific acknowledgements

Consortium memberships

Figures S1-10

Tables S1-13

Print summary for aap8757, *Analysis of Shared Heritability in Common Disorders of the Brain,* by Anttila V. et al.

Introduction

Disorders of the brain can exhibit considerable epidemiological comorbidity and share symptoms, provoking debate about their etiologic overlap. However, detailed study of phenotypes with different ages of onset, severity and presentation presents a considerable challenge. Recently developed heritability methods allow us to accurately measure correlation of genome-wide common variant risk between two phenotypes from pools of different individuals, to understand how connected they, or at least their genetic risks, are on the genomic level. We quantified the degree of overlap for genetic risk factors of 25 common brain disorders, based on genome-wide association data for 215,683 patients and 657,164 controls, as well as 17 phenotypes from a total of 1,191,588 individuals.

Rationale

The classification of brain disorders has evolved over the last century, reflecting the medical and scientific communities' assessments of the presumed root causes of clinical phenomena such as behavioral change, loss of motor function, or alterations of consciousness. Directly observable phenomena (such as the presence of emboli, protein tangles, or unusual electrical activity patterns) generally define and separate neurological disorders from psychiatric disorders. Understanding the genetic underpinnings and categorical distinctions for brain disorders and related phenotypes may inform the search for their biological mechanisms.

Results

Common variant risk for psychiatric disorders was shown to correlate significantly, especially between ADHD, bipolar disorder, major depressive disorder (MDD) and schizophrenia. In contrast, neurological disorders appear more distinct from one another and from the psychiatric disorders, except for migraine, which was significantly correlated to ADHD, MDD and Tourette Syndrome. We demonstrate that the personality trait neuroticism in the general population is significantly correlated with almost every psychiatric disorder and migraine. We also identify significant sharing between disorders and early life cognitive measures in the general population (e.g. years of education and college attainment), demonstrating positive correlation with several psychiatric disorders (e.g. anorexia nervosa and bipolar disorder) and negative correlation with several neurological phenotypes (e.g. Alzheimer's disease and ischemic stroke), even though the latter are considered to result from specific processes that occur later in life. Extensive simulations were also performed to inform how power, diagnostic misclassification and phenotypic heterogeneity influence genetic correlations.

Conclusion

The high degree of genetic correlation among many of the psychiatric disorders adds further evidence that the current clinical boundaries among them do not reflect distinct underlying pathogenic processes, at least on the genetic level. This suggests a deeply interconnected nature, in contrast to neurological disorders, and underscores the need to refine psychiatric diagnostics. Genetically informed analyses may provide important 'scaffolding' to support such restructuring of psychiatric nosology, which likely requires incorporating many levels of information. In contrast, we find limited evidence for widespread common genetic risk sharing among neurological disorders or across neurological and psychiatric disorders. We show that both psychiatric and neurological disorders have robust correlations with cognitive and personality measures. Further study is needed to evaluate whether overlapping genetic contributions to psychiatric pathology may influence treatment choices. Ultimately, such developments give hope to reducing heterogeneity and eventually improving the diagnosis and treatment of psychiatric disorders.

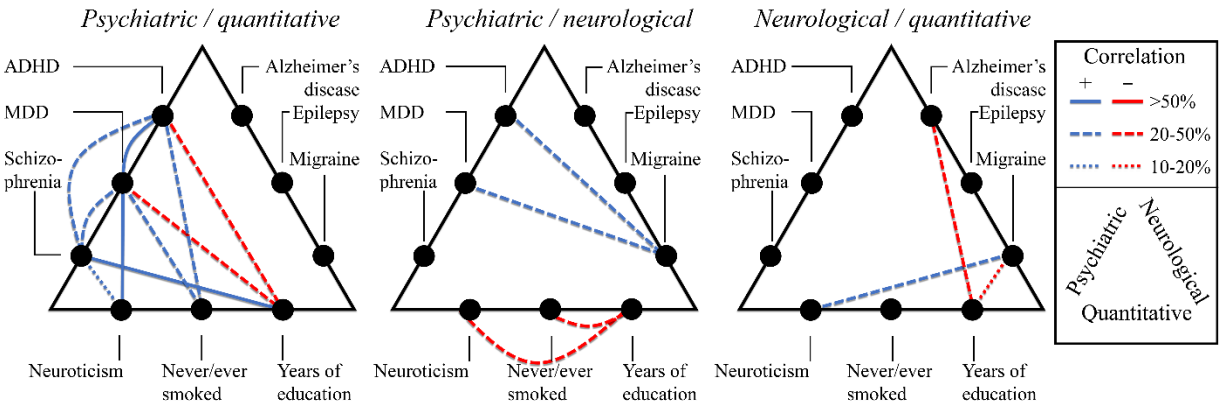
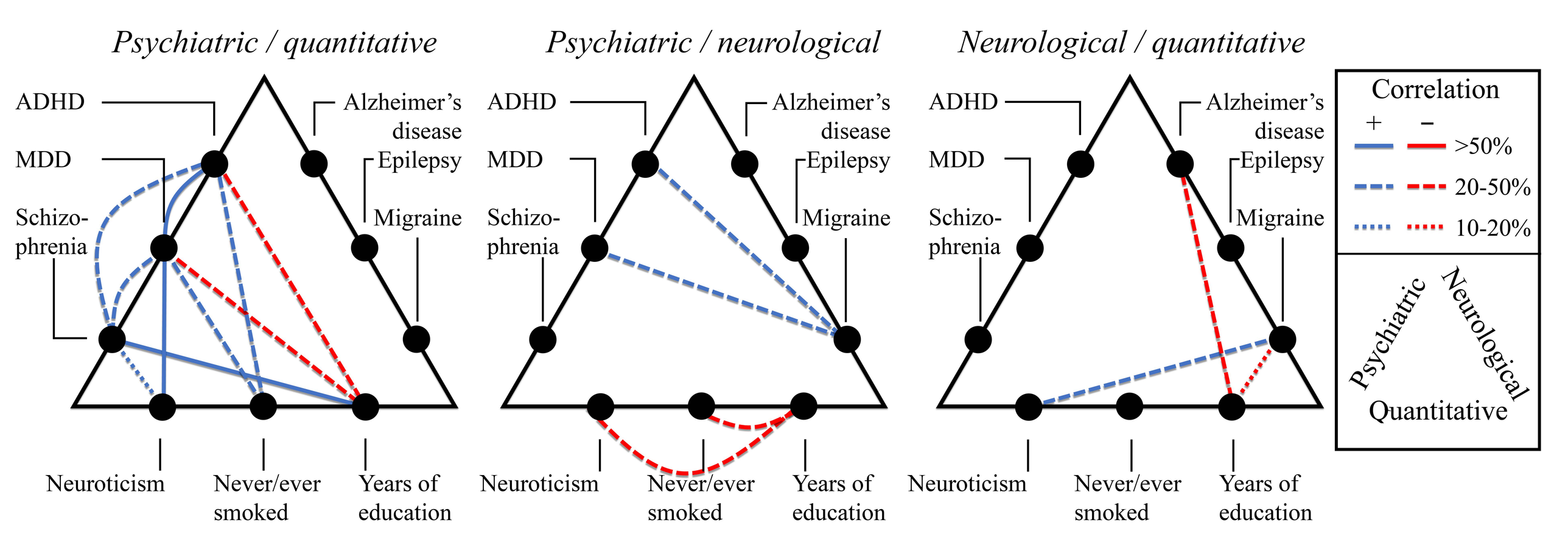


Figure Caption

Subsection of genetic risk correlations among brain disorders and quantitative phenotypes.

Heritability analysis of brain disorders points to pervasive sharing of genetic risk among psychiatric disorders, largely absent among neurological disorders, but present from both groups to neuro-cognitive quantitative phenotypes. Only significant correlations shown. Color and line solidity indicate direction and magnitude of correlation, respectively. ADHD – attention deficit hyperactivity disorder; MDD – major depressive disorder.


Psychiatric / quantitative
Psychiatric / neurological
Neurological / quantitative
ADHD
MDD
Schizo-
phrenia
Alzheimer's
disease
Epilepsy
Migraine
Neuroticism
Never/ever
smoked
Years of
education
Correlation
+
−
>50%
20-50%
10-20%
Psychiatric
Neurological
Quantitative

Supplementary Materials for

Analysis of Shared Heritability in Common Disorders of the Brain

Verneri Anttila…, Aiden Corvin, Benjamin M Neale, on behalf of the Brainstorm consortium

correspondence to:
verneri.anttila@gmail.com
acorvin@tcd.ie
bneale@broadinstitute.org

This PDF file includes:

Materials and Methods
Supplementary Text
Figs. S1-S10
Tables S1-6, S8-11

Other Supplementary Materials for this manuscript includes the following:

Tables S7, S12, S13 (separate files)

Materials and Methods

Data processing

We obtained GWAS meta-analysis summary statistics for 25 brain disorders and 17 phenotypes. Wherever non-European cohorts formed a part of those meta-analyses, we generated non-sex-stratified European-cohorts-only version of the meta-analysis of each disorder together with the primary analysts for each disorder to avoid bias stemming from ancestry differences. Prior to heritability analysis, each dataset underwent additional filtering: markers were excluded for not being present among the HapMap Project Phase 3 SNPs(*84*), having an allele mismatch to 1000 Genomes alleles, ambiguous strand information, INFO score <0.9 (where available), MAF<1%, and if considerable missingness in the meta-analysis was observed (where available; defined as effective per-SNP sample size less than two thirds of the 90th percentile of total sample size). To remove a potential source of bias, the major histocompatibility complex region (all SNPs on chromosome 6 between 25 and 35 Mb) was removed from all datasets, as was the region surrounding the APOE locus (all SNPs on chromosome 19 between 44 and 47 Mb) from the Alzheimer's disease summary data.

Simulations

To evaluate the robustness of these results under various scenarios, we performed various simulations using data from the UK Biobank(*85*). Details about the UK Biobank project are available at http://www.ukbiobank.ac.uk. Data for the current analyses were obtained under an approved data request (application number #18597).

We used data from the interim release of 152,376 samples, originally genotyped on the UK BiLEVE Axiom array and the UK Biobank Axiom array. We filtered individuals for Caucasian ancestry and recommended removals to arrive at a final dataset of 120,267 individuals. Simulated datasets were generated to evaluate the behavior of correlation estimates 1) under different degrees of misclassification; 2) under different heritability estimates for the two traits and 3) under different liability thresholds (232 simulation conditions, 100 replicates per condition, for a total of 2.95 billion simulated individuals).

In each simulation replicate, two sets of simulated quantitative phenotypes with heritability ranging from 5-50% and prevalence ranging from 1-10% (relevant to the study phenotypes) were generated by assigning 5% of total SNPs to have simulated effect sizes drawn from $N\left(0, \sqrt{\frac{h^2}{0.05\,M}}\right)$, where h^2 is the heritability and M is the total number of markers in the genome, standardized for minor allele frequency (p) by $\sqrt{2 * p * (1-p)}$. Individual phenotypes were simulated by calculating the sum of mean centered betas multiplied by the individual's risk alleles with the –score option in PLINK v1.90b3.38(*86*) and adding noise term e, drawn from $N(0, \sqrt{1-h^2})$, to achieve phenotypes which sum to $N(0, h^2)$. Dichotomous phenotypes were generated by assigning top 1%, 5% and 10% of each heritability simulation to be cases, and misclassification scenarios by mixing the simulated betas with those from a second, independently simulated phenotype in proportions ranging between 0-100%. Association statistics were created using an additive test in PLINK v1.90b3.38, and LDSC was used to calculate correlation estimates.

Simulation results were summarized to evaluate three specific scenarios considered relevant to the challenges (particularly for the psychiatric disorders, due to their spectrum-like behavior) in brain disorder co-morbidity:

1. *Effect of misclassification on phenotype heritability*. Given that we generally observe slightly lower heritability estimates in this study than reported in the literature with previous studies (which generally have used smaller, possibly less heterogeneous datasets), we generated 100 replicates each of simulated phenotypes at several prevalence and heritability values, and with varying degrees of misclassification of cases from a second, independent phenotype (Fig. S9A). These results demonstrate that while large-scale misclassification will impact the estimated heritability, very large misclassification proportions are required to by themselves give rise to large-scale changes in the observed heritability to the degree shown in Table S3.

2. *Effect of co-morbidity on genetic correlation*. Given the overlapping epidemiology of some phenotypes and the potential to observe false positive correlations due to non-trivial case misclassification, we created a range of phenotypes with varying mixing portions of correctly diagnosed cases (λ) and incorrectly diagnosed cases (1-λ) from an independent second phenotype and evaluated the genetic correlation between the hybrid phenotype and the second phenotype. This simulates the real-world scenario where e.g. (1-λ) proportion of bipolar cases would in fact be misclassified cases of schizophrenia free of bipolar disorder (Fig. S9B). We also derived a formula (see "Effect of co-morbidity and phenotypic misclassification on correlation estimates" below) to estimate the degree of misclassification required to produce the observed correlations in the absence of true genetic correlation (Table S6).

3. *Effect of bidirectional comorbidity on genetic correlation*. We expanded the simulation from the previous scenario given misclassification in both directions, i.e. where a proportion (1-λ) of bipolar disorder cases are misclassified schizophrenia cases and the same proportion of schizophrenia cases are misclassified bipolar disorder cases (Fig. S9C).

Power calculations

Using the same methodology as described for the simulations, we created 100 replicated pairs of datasets, each with varying sample sizes (10,000, 20,000 and 40,000 individuals with a 50/50 case/control split, randomly selected from the UK Biobank data; see section above), heritabilities (1%, 5%, 10% and 20%) and polygenicity (simulating 0.5%-100% of markers contributing to the heritability). In the second set of similarly created replicates, phenotypes were additionally created to be 10%, 20%, 30%, or 40% correlated to their pair in the first set. LDSC was used to calculate the correlation between the pair (Figure S10).

Heritability analysis

For a given trait, the total additive common SNP heritability in a set of GWAS summary statistics (h^2g) is estimated by regressing the association χ^2 statistic of a SNP against the total amount of common genetic variation tagged by that SNP (i.e., the sum of r^2 between that SNP and all surrounding SNPs within a 1 Mb window, termed the LD score). The LD scores themselves, for each SNP with MAF 5-50% in the Hapmap3 data, were obtained from previously published data(*87*) (https://github.com/bulik/ldsc) but

edited by removing the at the time erroneously included HLA region markers [chr6, 20-36 Mb]. Genetic correlations, r_g, (i.e., the genome-wide average shared genetic risk) for a pair of phenotypes was similarly estimated by regressing the product of Z-score for each phenotype for each SNP, instead of the χ^2 statistic. The LD score referenced above is estimated from a common reference panel (for this work, the European subset of the 1000 Genomes Project reference). In this framework, including LD in the regression allows us to distinguish and account for LD-independent error sources (such as sample sharing and population stratification) from LD-dependent sources, like polygenic signal). It is essential to use an approach which is not biased by sample overlaps when analyzing summary statistics, given the large amount of control sharing between the GWAS meta-analyses in the study. P-values and effect directions for each phenotype were used to create a set of directional χ^2 statistics, which were then regressed against the SNP LD scores (as the χ^2 statistic is dependent on the amount of variation tagged by the SNP).

A univariate regression of these statistics against the LD statistic of each SNP was used to estimate the heritability for each phenotype using LDSC v1.0.0(*88*). When converting the results to liability scale, we assumed that all controls were unselected for all brain disorders as well as coronary artery disease and Crohn's disease from the additional phenotypes (u = 1 for the formula presented in (*89*)). Phenotypes with a univariate heritability Z-score < 2 were excluded from further analysis (cardioembolic, large-, and small-vessel stroke and agreeableness personality measure), leaving 21 brain disorder phenotypes and 16 traits of interest. In the genetic correlation analysis, the product of χ^2 statistics from the two phenotypes was similarly regressed.

Significance was assessed by Bonferroni multiple testing correction by estimating the number of independent brain disorder phenotypes by matrix decomposition of the genetic correlation results using matSpD (see Links)(*90, 91*). The number of independent disorder phenotypes was estimated to be 17.7943 (from 22 initial disorders, after exclusions), yielding a Bonferroni-corrected threshold of $p < 3.35 \times 10^{-4}$ for disorder-disorder pairs; 12.1925 independent phenotypes (from 16 initial phenotypes, after exclusions) for a threshold of $p < 7.33 \times 10^{-4}$ for phenotype-phenotype pairs and a total of 216.96 disorder-phenotype pairs for a threshold of $p < 2.30 \times 10^{-4}$.

Functional enrichment and partitioning analysis

Partitioning analysis was conducted using LDSC v1.0.0(*88*), using stratified LD score regression to identify enriched cell type groups, expanding on the work described in Finucane et al(*92*). First, we obtained genome annotations for each of ten cell type groups, created by taking a union of regions with any of four histone modifications (H3K4me1, H3K4me3, H3K27ac, H3K9ac) in any cell type belonging to the cell type group. We then added each of these ten annotations to the full baseline model one at a time and performed LD score regression for each of the resulting ten models. For each of these ten analyses, we computed a Z-score for the regression coefficient corresponding to the cell type group, and we used this to test the hypothesis that the cell type group contributes positively to SNP heritability after controlling for the 53 categories in the full baseline model. Significance threshold was estimated from the number of independent phenotypes across 10 tissue categories and 53 functional categories (latter evaluated as 24 independent categories due to overlapping category structure) for Bonferroni thresholds

of $p < 2.81 \times 10^{-4}$ and 1.17×10^{-4}, respectively. For the behavioral-cognitive traits and additional traits, the corresponding thresholds were $p < 4.10 \times 10^{-4}$ and $p < 1.71 \times 10^{-4}$.

Correlation between heritability and dataset-specific factors

A weighted-least squares analysis was conducted among the brain disorder phenotypes in R, version 3.2, to determine what, if any, phenotype and dataset descriptive factors correlate with univariate heritability estimates. Weights were estimated using the squares of the standard errors of the univariate heritability estimates from the LD score regression analysis.

Supplementary text

Effect of co-morbidity and phenotypic misclassification on correlation estimates

We derived a formula to quantify the effect of case misclassification on the estimated genetic correlation between two traits, given the degree of misclassification, the observed heritability and the true genetic correlation. We assume both traits have similar sample and population prevalence.

Let λ be the fraction of correctly classified cases of phenotype 1, with the remainder being cases of phenotype 2 misclassified as cases of phenotype 1, β_1 and β_2 be true effects for phenotypes 1 and 2 on an arbitrary SNP. Therefore, the effect of the SNP on the misspecified phenotype 1 is α:

$$\alpha \equiv \lambda\beta_1 + (1-\lambda)\beta_2$$

Before considering the impact on the estimated genetic correlation, we note that this change in SNP effects means the heritability of the observed (potentially misclassified) phenotype may differ from the heritability of the true phenotype 1. Noting that the observed heritability for each phenotype is proportional to the variance of their effect sizes, we first calculate

$$\begin{aligned}\mathrm{Var}(\alpha) &= \mathrm{Var}\,(\lambda\beta_1 + (1-\lambda)\beta_2) \\ &= \lambda^2\,\mathrm{Var}\,(\beta_1) + 2\lambda(1-\lambda)\mathrm{Cov}(\beta_1,\beta_2) + (1-\lambda)^2\,\mathrm{Var}(\beta_2) \\ &= \lambda^2\,\mathrm{Var}\,(\beta_1) + 2\lambda(1-\lambda)r_g\sqrt{\mathrm{Var}(\beta_1)\,\mathrm{Var}(\beta_2)} + (1-\lambda)^2\,\mathrm{Var}(\beta_2)\end{aligned}$$

Then assuming standardized regression coefficients (e.g. following the LD score regression model), this can be written in terms of observed (obs) and true heritabilities for the two phenotypes and the number of genome-wide variants M as

$$\frac{h^2_{1,obs}}{M} = \lambda^2\frac{h_1^2}{M} + 2\lambda\,(1-\lambda)\,r_g\sqrt{\frac{h_1^2}{M}}\sqrt{\frac{h_2^2}{M}} + (1-\lambda)^2\,\frac{h_2^2}{M}$$

$$h^2_{1,obs} = \lambda^2 h_1^2 + 2\lambda\,(1-\lambda)\,r_g\sqrt{h_1^2 h_2^2} + (1-\lambda)^2 h_2^2$$

This allows solving for $\sqrt{h_1^2}$ using a quadratic equation,

$$0 = \lambda^2 h_1^2 + 2\lambda\,(1-\lambda)\, r_g \sqrt{h_1^2 h_2^2} + \,(1-\lambda)^2 h_2^2 - \, h_{1,obs}^2$$

$$\sqrt{h_1^2}_1 = \frac{-2\lambda(1-\lambda)\, r_g \sqrt{h_2^2} \,\pm\, \sqrt{4\lambda^2\,(1-\lambda)^2 r_g^2\, h_2^2 - 4\lambda^2\,\left[(1-\lambda)^2\, h_2^2 - \, h_{1,obs}^2\right]}}{2\lambda^2}$$

$$= \frac{-2\lambda(1-\lambda)\, r_g\, \sqrt{h_2^2} \,\pm\, 2\lambda \sqrt{(1-\lambda)^2\left(r_g^2 - 1\right) h_2^2 + \, h_{1,obs}^2}}{2\lambda^2}$$

$$= \frac{-(1-\lambda)\, r_g \sqrt{h_2^2} \,\pm \sqrt{(1-\lambda)^2\left(r_g^2 - 1\right) h_2^2 + \, h_{1,obs}^2}}{\lambda}$$

Note that the sign of the first term in the numerator will be opposite of the sign of r_g. Therefore if we select the sign of the phenotype so that $r_g > 0$, then we must add the second term to ensure $\sqrt{h_1^2} > 0$. This gives us

$$\sqrt{h_1^2} = \frac{-(1-\lambda)\, r_g \sqrt{h_2^2} + \sqrt{(1-\lambda)^2\left(r_g^2 - 1\right) h_2^2 + \, h_{1,obs}^2}}{\lambda}$$

Note that this will not be bounded above by one when λ is small. This is not surprising since a small λ implies that most of the cases reported for phenotype 1 are in fact cases for phenotype 2, making particular combinations of h_2^2, $h_{1,obs}^2$ and r_g infeasible for certain values of λ. From the above, the determinant of the quadratic form must be positive, thus

$$h_{1,obs}^2 \geq (1-\lambda)^2\left(1 - \, r_g^2\right) h_2^2$$

Similarly, the determinant of the quadratic formula, solving for h_2^2, implies

$$h_1^2 \leq \frac{h_{1,obs}^2}{\lambda^2\left(1 - \, r_g^2\right)}$$

This is the case unless no misclassification is present ($\lambda = 0$) or the phenotypes are functionally equivalent ($r_g^2 = 1$).

We can now return to the original question regarding the relationship between r_g and $r_{g,obs}$ in the presence of phenotype misclassification. We derive for the SNP effects of α and β_2:

$$r_{g,obs} \equiv \mathrm{Corr}(\alpha, \beta_2)$$
$$= \frac{\mathrm{Cov}\,(\alpha, \beta_2)}{\sqrt{\mathrm{Var}(\alpha)\mathrm{Var}(\beta_2)}}$$
$$= \frac{\mathrm{Cov}\,[\lambda\beta_1 + (1-\lambda)\beta_2, \beta_2]}{\sqrt{\mathrm{Var}(\alpha)\mathrm{Var}(\beta_2)}}$$

$$= \frac{\lambda \operatorname{Cov}(\beta_1, \beta_2) + (1-\lambda)\operatorname{Var}(\beta_2)}{\sqrt{\operatorname{Var}(\alpha)\operatorname{Var}(\beta_2)}}$$
$$= \frac{\lambda\, r_g \sqrt{\operatorname{Var}(\beta_1)\operatorname{Var}(\beta_2)} + (1-\lambda)\operatorname{Var}(\beta_2)}{\sqrt{\operatorname{Var}(\alpha)\operatorname{Var}(\beta_2)}}$$
$$= \lambda\, r_g \frac{\sqrt{\operatorname{Var}(\beta_1)}}{\sqrt{\operatorname{Var}(\alpha)}} + (1-\lambda)\frac{\sqrt{\operatorname{Var}(\beta_2)}}{\sqrt{\operatorname{Var}(\alpha)}}$$

Again assuming standardized regression coefficients, the variances can be written in terms of heritability as

$$r_{g,obs} = \frac{\lambda\, r_g \sqrt{h_1^2} + (1-\lambda)\sqrt{h_2^2}}{\sqrt{h_{1,obs}^2}}$$

Rearranging and substituting the expression for $\sqrt{h_1^2}$ from above, assuming $r_g > 0$, gives

$$r_g = \frac{r_{g,obs}\sqrt{h_{1,obs}^2} - (1-\lambda)\sqrt{h_2^2}}{\lambda\sqrt{h_1^2}}$$

$$= \frac{r_{g,obs}\sqrt{h_{1,obs}^2} - (1-\lambda)\sqrt{h_2^2}}{\lambda} \frac{\lambda}{-(1-\lambda)\, r_g\sqrt{h_2^2} + \sqrt{(1-\lambda)^2\left(r_g^2-1\right)h_2^2 + h_{1,obs}^2}}$$
$$= \frac{r_{g,obs}\sqrt{h_{1,obs}^2} - (1-\lambda)\sqrt{h_2^2}}{\sqrt{(1-\lambda)^2\left(r_g^2-1\right)h_2^2 + h_{1,obs}^2} - (1-\lambda)\, r_g\sqrt{h_2^2}}$$

Note that in the case with no misclassification, i.e. $\lambda = 1$,

$$r_g = \frac{r_{g,obs}\sqrt{h_{1,obs}^2}}{\sqrt{h_{1,obs}^2}} = r_{g,obs}$$

To examine the effects of co-morbidity has on the estimates, Table S5 shows numerical solutions for the estimated true correlation of some selected disorder pairs based on literature estimates of co-morbidity, assuming unidirectional misclassification and that $h_{1,obs}^2$ is equal to true h_1^2 (ie. that both disorders are roughly as heritable). For this table, we substituted the lambda values (see table for reference) and used the formula above to estimate what the true r_g would be, based on the observed r_g in this study. Figure S8 shows how the true genetic correlation estimates for those pairs behave across a range of λ values, given the observed r_g in this study, under the same assumptions as Table S5.

We further estimate what degree of unidirectional misclassification would be required to produce the significant r_g values we observe in the paper, in the absence of any true correlation. Given $r_g = 0$,

$$r_{g,obs} = \frac{(1-\lambda)\sqrt{h_2^2}}{h_{1,obs}^2}$$

$$\lambda = 1 - r_{g,obs}\frac{h_{1,obs}^2}{\sqrt{h_2^2}}$$

Table S6 lists the implied values of misclassification (1-λ) required to produce the observed significant r_g values between brain disorders in the study, if no true correlation between the phenotypes exists.

Study-specific acknowledgments

IGAP (Alzheimer's disease)

International Genomics of Alzheimer's Project (IGAP) is a large two-stage study based upon genome-wide association studies (GWAS) on individuals of European ancestry. In stage 1, IGAP used genotyped and imputed data on 7,055,881 single nucleotide polymorphisms (SNPs) to meta-analyze four previously-published GWAS datasets consisting of 17,008 Alzheimer's disease cases and 37,154 controls (The European Alzheimer's Disease Initiative, EADI [LabEx DISTALZ - Laboratory of Excellence for Development of Innovative Strategies for a Transdisciplinary approach to ALZheimer's disease]; the Alzheimer Disease Genetics Consortium, ADGC [UO1AG032984]; The Cohorts for Heart and Aging Research in Genomic Epidemiology consortium, CHARGE [R01AG033193]; The Genetic and Environmental Risk in AD consortium, GERAD [G0902227, MR/K013031/1, MR/L501517/1, ARUK-PG2014-1, MR/L023784/1, MR/M009076/1, SGR544:CADR]). This work was supported by the Framingham Heart Study's National Heart, Lung, and Blood Institute contract (N01-HC-25195; HHSN268201500001I), by grants (R01-AG016495, R01-AG008122, R01-AG033040) from the National Institute on Aging, grant (R01-NS017950) from the National Institute of Neurological Disorders and Stroke, as well as grants , P30AG10161, R01AG15819, R01AG17917, 1R01HL128914, 2R01HL092577, and 3R01HL092577-06S1. UK sample contribution was supported by the NIHR Queen Square Dementia Biomedical Research Unit. Funding of some samples was supported by the NIHR Biomedical Research Unit (Dementia) at University College London Hospitals NHS Foundation Trust.

IHGC (Migraine)

We would like to thank the numerous individuals who contributed to sample collection, storage, handling, phenotyping and genotyping within each of the individual cohorts. We also thank the important contribution to research made by the study participants. This work was supported by the National Human Genome Research Institute of the National Institutes of Health (grant number R44HG006981) for 23andme and the UK Medical Research Council and the Wellcome Trust (Grant ref: 102215/2/13/2) and the University of Bristol for ALSPAC. The Australian cohort was supported by National

Institutes of Health (NIH) Grants AA07535, AA07728, AA13320, AA13321, AA14041, AA11998, AA17688, DA012854, DA019951, AA010249, AA013320, AA013321, AA011998, AA017688, and DA027995; by Grants from the Australian National Health and Medical Research Council (NHMRC) (241944, 339462, 389927, 389875, 389891, 389892, 389938, 442915, 442981, 496739, 552485, 552498 and 1075175); by Grants from the Australian Research Council (ARC) (A7960034, A79906588, A79801419, DP0770096, DP0212016, and DP0343921); by the EU-funded GenomEUtwin (FP5-QLG2-CT- 2002- 01254) and ENGAGE (FP7- HEALTH- 201413) projects; and by the European Union's Seventh Framework program (2007–2013) under grant agreement no. 602633 (EUROHEADPAIN). DRN (FT0991022, 613674) and GWM (619667) were supported by the ARC Future Fellowship and NHMRC Fellowship Schemes. We thank P Visscher, D Duffy, A Henders, B Usher, E Souzeau, A Kuot, A McMellon, MJ Wright, MJ Campbell, A Caracella, L Bowdler, S Smith, B Haddon, A Conciatore, D Smyth, H Beeby, O Zheng and B Chapman for their input into project management, databases, phenotype collection, and sample collection, processing and genotyping. We acknowledge use of phenotype and genotype data from the British 1958 Birth Cohort DNA collection, funded by the Medical Research Council grant G0000934 and the Wellcome Trust grant 068545/Z/02. Genotyping for the B58C-WTCCC subset was funded by the Wellcome Trust grant 076113/B/04/Z. The B58C-T1DGC genotyping utilized resources provided by the Type 1 Diabetes Genetics Consortium, a collaborative clinical study sponsored by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Allergy and Infectious Diseases (NIAID), National Human Genome Research Institute (NHGRI), National Institute of Child Health and Human Development (NICHD), and Juvenile Diabetes Research Foundation International (JDRF) and supported by U01 DK062418. B58C-T1DGC GWAS data were deposited by the Diabetes and Inflammation Laboratory, Cambridge Institute for Medical Research (CIMR), University of Cambridge, which is funded by Juvenile Diabetes Research Foundation International, the Wellcome Trust and the National Institute for Health Research Cambridge Biomedical Research Centre; the CIMR is in receipt of a Wellcome Trust Strategic Award (079895). The B58C-GABRIEL genotyping was supported by a contract from the European Commission Framework Programme 6 (018996) and grants from the French Ministry of Research. The Danish HC study is funded by grants from The Advanced Technology Foundation (001-2009-2), The Lundbeck Foundation (R34-A3243), and The Lundbeck Foundation Initiative for Integrative Psychiatric Research (R102-A9118). The deCODE migraine study was funded in part by the European Commission (HEALTH-FP7-2013-Innovation-602891 to the NeuroPain Consortium) and the National Institute of Dental and Craniofacial Research (NIH R01DE022905). EGCUT received targeted financing from Estonian Research Council grant IUT20-60, Center of Excellence in Genomics (EXCEGEN) and University of Tartu (SP1GVARENG). We acknowledge EGCUT technical personnel, especially Mr V. Soo and S. Smit. Data analyses were carried out in part in the High Performance Computing Center of University of Tartu. For the Finnish MA cohort, the Wellcome Trust (grants WT089062 and 098051 to A.P.), the Academy of Finland (grants 200923, 251704, and 286500 to A.P., and 139795 to M.W.); the Academy of Finland Center of Excellence for Complex Disease Genetics; the EuroHead project (LSM-CT-2004-504837); the Academy of Finland, Center of Excellence in Complex

Disease Genetics, (grant numbers 213506 and 129680 to A.P. and J.K.); FP7-EUROHEADPAIN-no.602633, ENGAGE Consortium (grant agreement HEALTH-F4-2007-201413); EU/SYNSYS-Synaptic Systems (grant number 242167 to A.P.); the Sigrid Juselius Foundation, Finland (to A.P.); the Folkhälsan Research Foundation, Finland (to M.W.); Medicinska Understödsföreningen Liv & Hälsa (to M.W.), and the Helsinki University Central Hospital (to M.K., V.A.). German MA/MO (Munich): This study was supported by the Corona Foundation (S199/10052/2011). Health 2000: The Health 2000 survey was funded by the Finnish National Institute for Health and Welfare (THL) in collaboration with the National Social Insurance Institution and the five university hospital districts. VS was supported by the Academy of Finland, grant #139635, and the Finnish Foundation for Cardiovascular Research. The NFBC1966 sample received financial support from the Academy of Finland (project grants 104781, 120315, 129269, 1114194, 24300796, Center of Excellence in Complex Disease Genetics and SALVE), University Hospital Oulu, Biocenter, University of Oulu, Finland (75617), NHLBI grant 5R01HL087679-02 through the STAMPEED program (1RL1MH083268-01), NIH/NIMH (5R01MH63706:02), ENGAGE project and grant agreement HEALTH-F4-2007-201413, EU FP7 EurHEALTHAgeing -277849, the Medical Research Council, UK (G0500539, G0600705, G1002319, PrevMetSyn/SALVE) and the MRC, Centenary Early Career Award. The program is currently being funded by the H2020-633595 DynaHEALTH action and academy of Finland EGEA-project. For NTR/NESDA, we acknowledge the Netherlands Organisation for Scientific Research (NWO), the Netherlands Organisation for Health Research and Development (ZonMW), the EMGO+ Institute for Health and Care Research, the Neuroscience Campus Amsterdam, BBMRI–NL (184.021.007: Biobanking and Biomolecular Resources Research Infrastructure), the Avera Institute, Sioux Falls, South Dakota (USA), Rutgers University Cell and DNA Repository cooperative agreement [National Institute of Mental Health U24 MH068457-06], and the National Institutes of Health (NIH R01 HD042157-01A1, MH081802, Grand Opportunity grants 1RC2 MH089951 and 1RC2 MH089995). Part of the genotyping and analyses were funded by the Genetic Association Information Network (GAIN) of the Foundation for the National Institutes of Health. Genotyping was funded in part by grants from the National Institutes of Health (4R37DA018673-06, RC2 MH089951). The statistical analyses were carried out on the Genetic Cluster Computer (http://www.geneticcluster.org) which is supported by the Netherlands Scientific Organization (NWO 480-05-003), the Dutch Brain Foundation and the Department of Psychology and Education of the VU University Amsterdam. The Netherlands Twin register was also supported by ZonMW Addiction 31160008; ZonMW 940-37-024; NWO/SPI 56-464-14192; NWO-400-05-717; NWO-MW 904-61-19; NWO-MagW 480-04-004; NWO-Veni 016-115-035 and the European Research Council (ERC 230374, 284167). The Netherlands Study of Depression and Anxiety (NESDA) was also funded by ZonMW (Geestkracht program grant 10-000-1002). The generation and management of GWAS genotype data for the Rotterdam Study (RS I, RS II, RS III) was executed by the Human Genotyping Facility of the Genetic Laboratory of the Department of Internal Medicine, Erasmus MC, Rotterdam, The Netherlands. The GWAS datasets are supported by the Netherlands Organisation of Scientific Research NWO Investments (nr. 175.010.2005.011, 911-03-012), the Genetic Laboratory of the Department of Internal Medicine, Erasmus MC, the Research Institute for Diseases in the Elderly (014-93-015;

RIDE2), the Netherlands Genomics Initiative (NGI)/Netherlands Organisation for Scientific Research (NWO) Netherlands Consortium for Healthy Aging (NCHA), project nr. 050-060-810. We thank Pascal Arp, Mila Jhamai, Marijn Verkerk, Lizbeth Herrera and Marjolein Peters, MSc, and Carolina Medina-Gomez, MSc, for their help in creating the GWAS database, and Karol Estrada, PhD, Yurii Aulchenko, PhD, and Carolina Medina-Gomez, MSc, for the creation and analysis of imputed data. The Rotterdam Study is funded by Erasmus Medical Center and Erasmus University, Rotterdam, Netherlands Organization for the Health Research and Development (ZonMw), the Research Institute for Diseases in the Elderly (RIDE), the Ministry of Education, Culture and Science, the Ministry for Health, Welfare and Sports, the European Commission (DG XII), and the Municipality of Rotterdam. The authors are grateful to the study participants, the staff from the Rotterdam Study and the participating general practitioners and pharmacists. The Swedish Twin Registry acknowledges funding support from the Swedish Research Council, Swedish Brain Foundation, Karolinska Instutet Resarch Funds, and the Åke Wibergs Stiftelse. The WGHS is supported by HL043851 and HL080467 from the National Heart, Lung, and Blood Institute and CA047988 from the National Cancer Institute with collaborative scientific support and funding for genotyping provided by Amgen. Young Finns: The Young Finns Study has been financially supported by the Academy of Finland: grants 286284 (T.L.), 134309 (Eye), 126925, 121584, 124282, 129378 (Salve), 117787 (Gendi), and 41071 (Skidi); the Social Insurance Institution of Finland; Kuopio, Tampere and Turku University Hospital Medical Funds (grant X51001 for T.L.); Juho Vainio Foundation; Paavo Nurmi Foundation; Finnish Foundation of Cardiovascular Research (T.L.); Finnish Cultural Foundation; Tampere Tuberculosis Foundation (T.L.); Emil Aaltonen Foundation (T.L.); and Yrjö Jahnsson Foundation (T.L.). We gratefully acknowledge the THL DNA laboratory for its skilful work to produce the DNA samples used in this study, and Ville Aalto and Irina Lisinen for the expert technical assistance in the statistical analyses. Ester Cuenca-Leon is supported by a 'Beatriu de Pinós' grant (2010 BP-A and BP-A2) funded by AGAUR, Generalitat de Catalunya. Phil H. Lee is supported by NIMH K99 MH101367. Tune H. Pers is supported by the Alfred Benzon Foundation.

IPDGC (Parkinson’s disease)

We would like to thank all of the subjects who donated their time and biological samples to be a part of this study. This work was supported in part by the Intramural Research Programs of the National Institute of Neurological Disorders and Stroke (NINDS), the National Institute on Aging (NIA), and the National Institute of Environmental Health Sciences both part of the National Institutes of Health, Department of Health and Human Services; project numbers Z01-AG000949-02 and Z01-ES101986. In addition this work was supported by the Department of Defense (award W81XWH-09-2-0128), and The Michael J Fox Foundation for Parkinson’s Research. This work was supported by National Institutes of Health grants R01NS037167, R01CA141668, P50NS071674, American Parkinson Disease Association (APDA); Barnes Jewish Hospital Foundation; Greater St Louis Chapter of the APDA; Hersenstichting Nederland; Neuroscience Campus Amsterdam; and the section of medical genomics, the Prinses Beatrix Fonds. The KORA (Cooperative Research in the Region of Augsburg) research platform was started and financed by the Forschungszentrum für Umwelt und

Gesundheit, which is funded by the German Federal Ministry of Education, Science, Research, and Technology and by the State of Bavaria. This study was also funded by the German National Genome Network (NGFNplus number 01GS08134, German Ministry for Education and Research); by the German Federal Ministry of Education and Research (NGFN 01GR0468, PopGen); and 01EW0908 in the frame of ERA-NET NEURON and Helmholtz Alliance Mental Health in an Ageing Society (HA-215), which was funded by the Initiative and Networking Fund of the Helmholtz Association. The French GWAS work was supported by the French National Agency of Research (ANR-08-MNP-012). This study was also funded by France-Parkinson Association, the French program "Investissements d'avenir" funding (ANR-10-IAIHU-06) and a grant from Assistance Publique-Hôpitaux de Paris (PHRC, AOR-08010) for the French clinical data. This study was also sponsored by the Landspitali University Hospital Research Fund (grant to SSv); Icelandic Research Council (grant to SSv); and European Community Framework Programme 7, People Programme, and IAPP on novel genetic and phenotypic markers of Parkinson's disease and Essential Tremor (MarkMD), contract number PIAP-GA-2008-230596 MarkMD (to HP and JHu). This study utilized the high-performance computational capabilities of the Biowulf Linux cluster at the National Institutes of Health, Bethesda, Md. (http://biowulf.nih.gov), and DNA panels, samples, and clinical data from the National Institute of Neurological Disorders and Stroke Human Genetics Resource Center DNA and Cell Line Repository. People who contributed samples are acknowledged in descriptions of every panel on the repository website. We thank the French Parkinson's Disease Genetics Study Group and the Drug Interaction with genes (DIGPD) study group: Y Agid, M Anheim, A-M Bonnet, M Borg, A Brice, E Broussolle, J-C Corvol, P Damier, A Destée, A Dürr, F Durif, A Elbaz, D Grabil, S Klebe, P. Krack, E Lohmann, L. Lacomblez, M Martinez, V Mesnage, P Pollak, O Rascol, F Tison, C Tranchant, M Vérin, F Viallet, and M Vidailhet. We also thank the members of the French 3C Consortium: C Berr, C Tzourio, and P Amouyel for allowing us to use part of the 3C cohort, and D Zelenika for support in generating the genome-wide molecular data. We thank P Tienari (Molecular Neurology Programme, Biomedicum, University of Helsinki), T Peuralinna (Department of Neurology, Helsinki University Central Hospital), L Myllykangas (Folkhalsan Institute of Genetics and Department of Pathology, University of Helsinki), and R Sulkava (Department of Public Health and General Practice Division of Geriatrics, University of Eastern Finland) for the Finnish controls (Vantaa85+ GWAS data). We used genome-wide association data generated by the Wellcome Trust Case-Control Consortium 2 (WTCCC2) from UK patients with Parkinson's disease and UK control individuals from the 1958 Birth Cohort and National Blood Service. Genotyping of UK replication cases on ImmunoChip was part of the WTCCC2 project, which was funded by the Wellcome Trust (083948/Z/07/Z). UK population control data was made available through WTCCC1. This study was supported by the Medical Research Council and Wellcome Trust disease centre (grant WT089698/Z/09/Z to NW, JHa, and ASc). As with previous IPDGC efforts, this study makes use of data generated by the Wellcome Trust Case-Control Consortium. A full list of the investigators who contributed to the generation of the data is available from www.wtccc.org.uk. Funding for the project was provided by the Wellcome Trust under award 076113, 085475 and 090355. This study was also supported by Parkinson's UK (grants 8047 and J-0804) and the Medical Research Council (G0700943). We thank

Jeffrey Barrett for assistance with the design of the ImmunoChip. DNA extraction work that was done in the UK was undertaken at University College London Hospitals, University College London, who received a proportion of funding from the Department of Health's National Institute for Health Research Biomedical Research Centres funding. This study was supported in part by the Wellcome Trust/Medical Research Council Joint Call in Neurodegeneration award (WT089698) to the Parkinson's Disease Consortium (UKPDC), whose members are from the UCL Institute of Neurology, University of Sheffield, and the Medical Research Council Protein Phosphorylation Unit at the University of Dundee. The MRC (JPND), Parkinsons UK and the NIHR UCLH Biomedical Research centre are gratefully acknowledged (NWW)

METASTROKE consortium of the International Stroke Genetics Consortium (Ischemic stroke)

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreements No 666881, SVDs@target (to M Dichgans) and No 667375, CoSTREAM (to M Dichgans); the DFG as part of the Munich Cluster for Systems Neurology (EXC 1010 SyNergy) and the CRC 1123 (B3)(to M Dichgans); the Corona Foundation (to M Dichgans); the Fondation Leducq (Transatlantic Network of Excellence on the Pathogenesis of Small Vessel Disease of the Brain)(to M Dichgans); the e:Med program (e:AtheroSysMed) (to M Dichgans) and the FP7/2007-2103 European Union project CVgenes@target (grant agreement number Health-F2-2013-601456) (to M Dichgans).

Eating Disorders Working Group of the Psychiatric Genomics Consortium (Anorexia nervosa)

Data on anorexia nervosa were made possible by funding for the Genetic Consortium on Anorexia Nervosa by the Wellcome Trust Case Control Consortium 3 project titled "A Genome-Wide Association Study of Anorexia Nervosa" (WT088827/Z/09) and the Foundation of Hope, Raleigh, North Carolina, USA. Funding for the Children's Hospital of Pennsylvania and Price Foundation study was from the Price Foundation, the Klarman Family Foundation, Scripps Translational Sciences Institute Clinical Translational Science Award [Grant Number U54 RR0252204-01], Institute Development Award to the Center for Applied Genomics from the CHOP; 2011 - 2014 Davis Foundation Postdoctoral Fellowship Program in Eating Disorders Research Award, Yiran Guo; 2012 - 2015 Davis Foundation Postdoctoral Fellowship Program in Eating Disorders Research Award, Dong Li.

Major Depressive Disorder Working Group of the Psychiatric Genomics Consortium

This work was funded by the German Research Foundation (DFG, grant FOR2107 DA1151/5-1 to UD; SFB-TRR58, Project C09 to UD) and the Interdisciplinary Center for Clinical Research (IZKF) of the medical faculty of Münster (grant Dan3/012/17 to UD).

Tourette Syndrome and Obsessive Compulsive Disorder Working Group of the Psychiatric Genomics Consortium (Tourette Syndrome and Obsessive Compulsive Disorder)

This study was supported by Grants from the National Institute of Mental Health [R01MH092290; R01MH092291; R01MH092292; R01MH092293; R01MH092513; R01MH092516; R01MH092520; R01MH092289; U24MH068457] and the New Jersey Center for Tourette Syndrome and Associated Disorders (NJCTS).

Consortium memberships

IGAP (Alzheimer's disease)

Benjamin Grenier-Boley, Vincent Chouraki, Yoichiro Kamatani, Marie-Thérèse Bihoreau, Florence Pasquier, Olivier Hanon, Dominique Campion, Claudine Berr, Luc Letenneur, Nathalie Fievet, Alexis Brice, Didier Hannequin, Karen Ritchie, Jean-Francois Dartigues, Christophe Tzourio, Philippe Amouyel, Anne Boland, Jean-François Deleuze, Jacques Epelbaum, Emmanuelle Duron, Bruno Dubois, Adam C. Naj, Gyungah Jun, Gary W. Beecham, Badri N. Vardarajan, Brian Kunkle, Christiane Reitz, Joseph D. Buxbaum, Paul K. Crane, Philip L. De Jager, Alison M. Goate, Matthew J. Huentelman, M. Ilyas Kamboh, Eric B. Larson, Oscar L. Lopez, Amanda J. Myers, Ekaterina Rogaeva, Peter St George-Hyslop, Debby W. Tsuang, John R. Gilbert, Hakon Hakonarson, Duane Beekly, Kara L. Hamilton-Nelson, Kelley M. Faber, Laura B. Cantwell, Deborah Blacker, David A. Bennett, Tatiana M. Foroud, Walter A. Kukull, Kathryn L. Lunetta, Eden R. Martin, Li-San Wang, Richard Mayeux, Jonathan L. Haines, Margaret A. Pericak-Vance, Lindsay A. Farrer, Gerard D. Schellenberg, Deborah C. Mash, Roger L. Albin, Liana G. Apostolova, Steven E. Arnold, Clinton T. Baldwin, Lisa L. Barnes, Thomas G. Beach, Thomas D. Bird, Bradley F. Boeve, James D. Bowen, James R. Burke, Minerva M. Carrasquillo, Steven L. Carroll, Lori B. Chibnik, David G. Clark, Carlos Cruchaga, Charles DeCarli, F. Yesim Demirci, Malcolm Dick, Kenneth B. Fallon, Martin R. Farlow, Steven Ferris, Douglas R. Galasko, Piyush Gampawar, Yasaman Saba, Marla Gearing, Daniel H. Geschwind, Neill R. Graff-Radford, Ronald L. Hamilton, John Hardy, Elizabeth Head, Lawrence S. Honig, Christine M. Hulette, Bradley T. Hyman, Gail P. Jarvik, Gregory A. Jicha, Lee-Way Jin, Anna Karydas, John S.K. Kauwe, Jeffrey A. Kaye, Ronald Kim, Edward H. Koo, Neil W Kowall, Frank M. LaFerla, James B. Leverenz, Allan I. Levey, Ge Li, Andrew P. Lieberman, Constantine G. Lyketsos, Wayne C. McCormick, Susan M. McCurry, Carol A. Miller, Jill R. Murrell, John M. Olichney, Vernon S. Pankratz, Aimee Pierce, Wayne W. Poon, Joseph F. Quinn, Murray Raskind, Barry Reisberg, Erik D. Roberson, Mary Sano, Andrew J. Saykin, Julie A. Schneider, Lon S. Schneider, William W. Seeley, Helena Schmidt, Albert V. Smith, Amanda G. Smith, Joshua A. Sonnen, Salvatore Spina, Robert A. Stern, Rudolph E. Tanzi, John Q. Trojanowski, Vivianna M. Van Deerlin, Linda J. Van Eldik, Sandra Weintraub, Kathleen A. Welsh-Bohmer, Randall L. Woltjer, Chang-En Yu, Robert Barber, Denise Harold, Rebecca Sims, Giancarlo Russo, Nicola Jones, Melanie L Dunstan, Alfredo Ramirez, Janet A Johnston, David C Rubinsztein, Michael Gill, John Gallacher, Anthony Bayer, Magda Tsolaki, Petra Proitsi, John Collinge, Nick C Fox, John Hardy, Robert Clarke, Carol Brayne, Susanne Moebus, Wolfgang Maier, Harald Hampel, Sabrina Pichler, Alison Goate, Minerva M Carrasquillo, Steven G Younkin, Michael J Owen, Michael C O'Donovan, Simon Mead, Peter Passmore, Kevin Morgan, John F Powell, John S.K.

Kauwe, Carlos Cruchaga, Matthias Riemenschneider, Markus M Nöthen, Lesley Jones, Peter A Holmans, Valentina Escott-Price, Julie Williams, Patrick G Kehoe, Jason D Warren, Jonathan M Schott, Natalie Ryan, Martin Rossor, Yoav Ben-Shlomo, Michelle Lupton, Steffi Riedel-Heller, Martin Dichgans, Reiner Heun, Per Hoffmann, Johannes Kornhuber, Hendrik van den Bussche, Brian Lawlor, Aoibhinn Lynch, David Mann, Isabella Heuser, Lutz Frölich, John C Morris, Andrew McQuillin, Ammar Al-Chalabi, Christopher E Shaw, Andrew B Singleton, Rita Guerreiro, Karl-Heinz Jöckel, H-Erich Wichmann, Dennis W Dickson, Ronald C Petersen, Carla A Ibrahim-Verbaas, Anita L DeStefano, Joshua C Bis, M. Arfan Ikram, Agustin Ruiz, Seung-Hoan Choi, Vilmundur Gudnason, Najaf Amin, Oscar L Lopez, Gudny Eiriksdottir, Thomas H Mosley, Jr., Tamara B Harris, Jerome I Rotter, Michael A Nalls, Palmi V Jonsson, Mercè Boada, Albert Hofman, Lenore J Launer, Cornelia M van Duijn, Sudha Seshadri, Alexa Beiser, Stephanie Debette, Qiong Yang, Galit Weinstein, Jing Wang, Andre G Uiterlinden, Peter J Koudstaal, William T Longstreth, Jr, James T Becker, Thomas Lumley, Kenneth Rice, Peter Dal-Bianco, Gerhard Ransmayr, Thomas Benke, Sven van der Lee, Jan Bressler, Myriam Fornage, Isabel Hernández, Ana Mauleón and Montserrat Alegret

IHGC (Migraine)

Padhraig Gormley, Verneri Anttila, Bendik S Winsvold, Priit Palta, Tonu Esko, Kai-How Farh, Ester Cuenca-Leon, Mikko Muona, Nicholas A Furlotte, Tobias Kurth, George McMahon, Lannie Ligthart, Gisela M Terwindt, Mikko Kallela, Rainer Malik, Caroline Ran, Scott G Gordon, Stacy Steinberg, Guntram Borck, Markku Koiranen, Hieab Adams, Terho Lehtimäki, Antti-Pekka Sarin, Juho Wedenoja, Lydia Quaye, David A Hinds, Julie E Buring, Markus Schürks, Paul M Ridker, Maria Gudlaug Hrafnsdottir, Jouke-Jan Hottenga, Brenda WJH Penninx, Markus Färkkilä, Ville Artto, Mari Kaunisto, Salli Vepsäläinen, Tobias M Freilinger, Pamela A F Madden, Nicholas G Martin, Grant W Montgomery, Eija Hamalainen, Hailiang Huang, Lude Franke, Jie Huang, Evie Stergiakouli, Phil H Lee, Cynthia Sandor, Caleb Webber, Zameel Cader, Bertram Muller-Myhsok, Stefan Schreiber, Thomas Meitinger, Johan Eriksson, Veikko Salomaa, Kauko Heikkilä, Elizabeth Loehrer, Andre G Uitterlinden, Albert Hofman, Cornelia M van Duijn, Lynn Cherkas, Audun Stubhaug, Christopher S Nielsen, Minna Männikko, Evelin Mihailov, Lili Milani, Hartmut Göbel, Ann-Louise Esserlind, Anne Francke Christensen, Thomas Folkmann Hansen, Thomas Werge, Bru Cormand, Lyn Griffiths, Marjo Hiekkala, Alfons Macaya, Patricia Pozo-Rosich, Jaakko Kaprio, Arpo J Aromaa, Olli Raitakari, M Arfan Ikram, Tim Spector, Marjo-Riitta Järvelin, Andres Metspalu, Christian Kubisch, David P Strachan, Michel D Ferrari, Andrea C Belin, Martin Dichgans, Maija Wessman, Arn MJM van den Maagdenberg, John-Anker Zwart, Dorret I Boomsma, George Davey Smith, Nicholas Eriksson, Mark J Daly, Benjamin M Neale, Jes Olesen, Daniel I. Chasman, Dale R Nyholt and Aarno Palotie

ILAE Consortium on Complex Epilepsies (Epilepsy)

Richard Anney, Andreja Avbersek, Larry Baum, Felicitas Becker, Samuel Berkovic, Jonathan Bradfield, Russell Buono, Claudia B. Catarino, Gianpiero Cavalleri, Stacey Cherny, Alison Coffey, Patrick Cossette, Gerrit-Jan Haan, Peter Jonghe, Carolien Kovel, Chantal Depondt, Dennis Dlugos, Colin Doherty, Thomas Ferraro, Martha Feucht, Andre Franke, Jacqueline French, Verena Gaus, Hongsheng Gui, Youling Guo, Hakon

Hakonarson, Erin Heinzen, Ingo Helbig, Helle Hjalgrim, Jennifer Jamnadas-Khoda, Michael Johnson, Reetta Kälviäinen, Anne-Mari Kantanen, Dalia Kasperaviciute, Dorothee Trenite, Bobby Koeleman, Wolfram Kunz, Patrick Kwan, Yu Lau, Holger Lerche, Costin Leu, Wolfgang Lieb, Dick Lindhout, Warren Lo, Daniel Lowenstein, Alberto Malovini, Anthony Marson, Mark McCormack, James Mills, Martina Moerzinger, Rikke Møller, Anne Molloy, Hiltrud Muhle, Ping-Wing Ng, Markus M. Nöthen, Terence O'Brien, Karen Oliver, Aarno Palotie, Michael Privitera, Rodney Radtke, Philipp Reif, Ann-Kathrin Ruppert, Thomas Sander, Theresa Scattergood, Steven Schachter, Christoph Schankin, Ingrid Scheffer, Bettina Schmitz, Susanne Schoch, Pak Sham, Sanjay Sisodiya, David Smith, Philip Smith, Michael Sperling, Michael Steffens, Pasquale Striano, Hans Stroink, Rainer Surges, Meng Tan, Neil G. Thomas, Marian Todaro, Holger Trucks, Frank Visscher, Nicole Walley, Zhi Wei, Christopher D. Whelan, Wanling Yang, Federico Zara and Fritz Zimprich

IMSGC (Multiple sclerosis)
Chris Cotsapas

IPDGC (Parkinson's disease)
Jose Bras, Alexis Brice, Boniface Mok, Valentina Escott-Price, Thomas Foltynie, Thomas Gasser, Raphael Gibbs, Rita Guerreiro, John Hardy, Dena Hernandez, Peter Heutink, Peter Holmans, Suzanne Lesage, Steven Lubbe, Maria Martinez, Niccolo Mencacci, Huw Morris, Michael Nalls, Claudia Schulte, Manu Sharma, Mina Ryten, Joshua Shulman, Javier Simón-Sánchez, Andrew Singleton, Nigel Williams and Nick Wood

METASTROKE consortium of the International Stroke Genetics Consortium (Ischemic stroke)
Rainer Malik, Matthew Traylor, Sara Pulit, Steve Bevan, Jemma Hopewell, Elizabeth Holliday, Wei Zhao, Philippe Amouyel, John Attia, Thomas Battey, Klaus Berger, Giorgio Boncoraglio, Ganesh Chauhan, Wei-Min Chen, Ioana Cotlarciuc, Stephanie Debette, Guido Falcone, Andreea Ilinca, Steven Kittner, Christina Kourkoulis, Robin Lemmens, Arne Lindgren, James Meschia, Braxton Mitchell, Joana Pera, Peter Rothwell, Pankaj Sharma, Cathie Sudlow, Turgut Tatlisumak, Vincent Thijs, Astrid Vicente, Daniel Woo, Sudha Seshadri, Jonathan Rosand, Hugh Markus, Bradford Worrall and Martin Dichgans

International Stroke Genetics Consortium Study of Intracerebral Hemorrhage (Intracerebral Hemorrhage)
Miriam Raffeld, Guido Falcone, David Tirschwell, Bradford Worrall, Agnieszka Slowik, Magdy Selim, Jordi Jimenez-Conde, Daniel Woo, Scott Silliman, Arne Lindgren, James Meschia, Rainer Malik, Martin Dichgans and Jonathan Rosand

Attention-Deficit Hyperactivity Disorder Working Group of the Psychiatric Genomics Consortium (Attention-deficit hyperactivity disorder)
Stephen V. Faraone, Bru Cormand, Josep Antoni Ramos-Quiroga, Cristina Sánchez-Mora, Marta Ribasés, Miguel Casas, Amaia Hervas, Maria Jesús Arranz, Yufeng Wang,

Jan Haavik, Tetyana Zayats, Stefan Johansson, Carol Mathews, Nigel Williams, Peter Holmans, Joanna Martin, Hakon Hakonarson, Josephine Elia, Tobias J Renner, Benno G Schimmelmann, Anke Hinney, Özgür Albayrak, Johannes Hebebrand, André Scherag, Astrid Dempfle, Beate Herpertz-Dahlmann, Judith Sinzig, Gerd Lehmkuhl, Aribert Rothenberger, Edmund J S Sonuga-Barke, Hans-Christoph Steinhausen, Jonna Kuntsi, Philip Asherson, Robert D. Oades, Tobias Banaschewski, Herbert Roeyers, Joseph Sergeant, Richard P. Ebstein, Sarah Hohmann, Barbara Franke, Jan K. Buitelaar, Lindsey Kent, Alejandro Arias Vasquez, Michael Gill, Nanda Lambregts-Rommelse, Richard JL Anney, Aisling Mulligan, Joseph Biederman, Yanli Zhang-James, Alysa E. Doyle, Andreas Reif, Klaus-Peter Lesch, Andreas Warnke, Christine M. Freitag, Susanne Walitza, Olga Rivero, Haukur Palmason, Jobst Meyer, Marcel Romanos, Anita Thapar, Kate Langley, Michael C. O'Donovan, Michael J. Owen, Marcella Rietschel, Stephanie H Witt, Soeren Dalsgaard, Preben Bo Mortensen, Anders Børglum, Ditte Demontis, Joel Gelernter, Irwin Waldman, Joel Nigg, Beth Wilmot, Nikolas Molly, Luis Rohde, Claiton Bau, Eugenio Grevet, Mara Hutz, Nina Roth Mota, Eric Mick, Sarah E. Medland, Benjamin M Neale, Raymond Walters, Mark J. Daly, Stephan Ripke, Alice Charach, Russell Schachar, Jennifer Crosbie, Sandra K. Loo, Susan L. Smalley and James J. McGough

Autism Spectrum Disorders Working Group of the Psychiatric Genomics Consortium (Autism)

Richard Anney, Stephan Ripke, Verneri Anttila, Peter Holmans, Hailiang Huang, Phil H Lee, Sarah Medland, Benjamin Neale, Elise Robinson, Lauren Weiss, Joana Almeida, Evdokia Anagnostou, Elena Bacchelli, Joel Bader, Anthony Bailey, Vanessa Bal, Agatino Battaglia, Raphael Bernier, Catalina Betancur, Sven Bölte, Patrick Bolton, Sean Brennan, Rita Cantor, Patrícia Celestino-Soper, Andreas G. Chiocchetti, Michael Cuccaro, Geraldine Dawson, Maretha De Jonge, Silvia De Rubeis, Richard Delorme, Frederico Duque, Sean Ennis, A. Gulhan Ercan-Sencicek, Eric Fombonne, Christine M. Freitag, Louise Gallagher, John Gilbert, Arthur Goldberg, Andrew Green, Dorothy Grice, Stephen Guter, Jonathan Haines, Robert Hendren, Christina Hultman, Sabine mKlauck, Alexander Kolevzon, Christine Ladd-Acosta, Marion Leboyer, David Ledbetter, Christa Lese Martin, Pat Levitt, Jennifer Lowe, Elena Maestrini, Tiago Magalhaes, Shrikant Mane, Donna Martin, William McMahon, Alison Merikangas, Nancy Minshew, Anthony Monaco, Daniel Moreno-De-Luca, Eric Morrow, John Nurnberger, Guiomar Oliveira, Jeremy Parr, Margaret Pericak-Vance, Dalila Pinto, Regina Regan, Karola Rehnström, Abraham Reichenberg, Kathryn Roeder, Bernadette Rogé, Guy Rouleau, Sven Sandin, Gerard Schellenberg, Stephen Scherer, Stacy Steinberg, Astrid Vicente, Jacob Vorstman, Regina Waltes, Thomas Wassink, Ellen Wijsman, A. Jeremy Willsey, Lonnie Zwaigenbaum, Timothy Yu, Joseph Buxbaum, Edwin Cook, Hilary Coon, Daniel Geschwind, Michael Gill, Hakon Hakonarson, Joachim Hallmayer, Aarno Palotie, Susan Santangelo, James Sutcliffe, Dan Arking and Mark Daly

Bipolar Disorders Working Group of the Psychiatric Genomics Consortium (Bipolar disorder)

Marcella Rietschel, Thomas G Schulze, Jana Strohmaier, Robert C Thompson, Stephanie H Witt, John Strauss, James L Kennedy, John B Vincent, Keith Matthews,

Shaun Purcell, Douglas Ruderfer, Pamela Sklar, Jordan Smoller, Laura J Scott, Margit Burmeister, Devin Absher, William E Bunney, Huda Akil, Ole A Andreassen, Srdjan Djurovic, Morten Mattingsdal, Ingrid Melle, Gunnar Morken, Aiden Corvin, Michael Gill, Derek Morris, Adebayo Anjorin, Nick Bass, Andrew McQuillin, Douglas Blackwood, Andrew McIntosh, Alan W McLean, Walter J Muir, Sarah E Bergen, Vishwajit Nimgaonkar, Marian L Hamshere, Christina Hultman, Mikael Landén, Paul Lichtenstein, Patrick Sullivan, Martin Schalling, Louise Frisén, Shaun Purcell, Eli Stahl, Amanda Dobbyn, Laura Huckins, Stéphane Jamain, Marion Leboyer, Bruno Etain, Frank Bellivier, Andreas J Forstner, Markus Leber, Stefan Herms, Per Hoffmann, Anna Maaser, Sascha B Fischer, Céline S Reinbold, Sarah Kittel-Schneider, Jolanta Lissowska, Janice M Fullerton, Joanna Hauser, Sarah E Medland, Scott D Gordon, Jens Treutlein, Josef Frank, Fabian Streit, José Guzman-Parra, Fermin Mayoral, Piotr M Czerski, Neonila Szeszenia-Dabrowska, Bertram Müller-Myhsok, Markus Schwarz, Peter R Schofield, Nicholas G Martin, Grant W Montgomery, Mark Lathrop, Bernhard T Baune, Sven Cichon, Thomas W Mühleisen, Franziska Degenhardt, Manuel Mattheisen, Johannes Schumacher, Wolfgang Maier, Markus M Nöthen, Michael Bauer, Philip B Mitchell, Andreas Reif, Tiffany A Greenwood, Caroline M Nievergelt, Paul D Shilling, Nicholas J Schork, Erin N Smith, John I Nurnberger, Howard J Edenberg, Tatiana Foroud, Elliot S Gershon, William B Lawson, Evaristus A Nwulia, Maria Hipolito, John Rice, William Byerley, Francis J McMahon, Wade Berrettini, James B Potash, Peter P Zandi, Sebastian Zöllner, Peng Zhang, Gerome Breen, Lisa Jones, Peter A Holmans, Ian R Jones, George Kirov, Valentina Escott-Price, Ivan Nikolov, Michael C O'Donovan, Michael J Owen, Nick Craddock, I Nicol Ferrier, Martin Alda, Pablo Cervantes, Cristiana Cruceanu, Guy A. Rouleau, Gustavo Turecki, Qingqin Li, Roel Ophoff, Rolf Adolfsson, Carlos Pato and Joanna M Biernacka

Eating Disorder Working Group of the Psychiatric Genomics Consortium (Anorexia Nervosa)

Harry Brandt, Scott Crow, Manfred M. Fichter, Katherine A. Halmi, Maria La Via, James Mitchell, Michael Strober, Alessandro Rotondo, D. Blake Woodside, Pamela Keel, Lisa Lilenfeld, Andrew W. Bergen, Walter Kaye, Pierre Magistretti, Deborah Kaminska, Vesna Boraska Perica, Christopher S. Franklin, James A. B. Floyd, Laura M. Thornton, Laura M. Huckins, Lorraine Southam, N. William Rayner, Ioanna Tachmazidou, Kelly L. Klump, Janet Treasure, Cathryn M. Lewis, Ulrike Schmidt, Federica Tozzi, Kirsty Kiezebrink, Johannes Hebebrand, Philip Gorwood, Roger A. H. Adan, Martien J. H. Kas, Angela Favaro, Paolo Santonastaso, Fernando Fernández-Aranda, Monica Gratacos, Filip Rybakowski, Jaakko Kaprio, Anna Keski-Rahkonen, Anu Raevuori, Eric F. van Furth, Margarita C. T. Slof-Op 't Landt, James I. Hudson, Ted Reichborn-Kjennerud, Gun Peggy S. Knudsen, Palmiero Monteleone, Allan S. Kaplan, Andreas Karwautz, Hakon Hakonarson, Wade H. Berrettini, Yiran Guo, Dong Li, Nicholas J. Schork, Tetsuya Ando, Tõnu Esko, Krista Fischer, Katrin Mannik, Andres Metspalu, Jessica H. Baker, Roger D. Cone, Janiece E. DeSocio, Christopher E. Hilliard, Julie K. O'Toole, Jacques Pantel, Jin Peng Szatkiewicz, Chrysecolla Taico, Stephanie Zerwas, Sara E. Trace, Oliver S. P. Davis, Sietske Helder, Roland Burghardt, Martina de Zwaan, Karin Egberts, Stefan Ehrlich, Beate Herpertz-Dahlmann, Wolfgang Herzog, Hartmut Imgart, André Scherag, Susann Scherag, Stephan Zipfel, Nicolas Ramoz, Unna N. Danner, Carolien de Kove,

Judith Hendriks, Bobby P.C. Koeleman, Roel A. Ophoff, Annemarie A. van Elburg, Maurizio Clementi, Daniela Degortes, Monica Forzan, Elena Tenconi, Elisa Docampo, Susana Jimenez-Murcia, Jolanta Lissowska, Neonilia Szeszenia-Dabrowska, Joanna Hauser, Leila Karhunen, Ingrid Meulenbelt, P. Eline Slagboom, Steve Crawford, Alfonso Tortorella, Mario Maj, George Dedoussis, Fragiskos Gonidakis, Konstantinos Tziouvas, Artemis Tsitsika, Hana Papežová, Lenka Slachtova, Debora Martaskova, James L. Kennedy, Robert D. Levitan, Zeynep Yilmaz, Julia Huemer, Gudrun Wagner, Paul Lichtenstein, Gerome Breen, Sarah Cohen-Woods, Sven Cichon, Ina Giegling, Stefan Herms, Dan Rujescu, Stefan Schreiber, H-Erich Wichmann, Christian Dina, Giovanni Gambaro, Nicole Soranzo, Antonio Julia, Sara Marsal, Raquel Rabionet, Danielle M. Dick, Aarno Palotie, Samuli Ripatti, Ole A. Andreassen, Thomas Espeseth, Astri Lundervold, Ivar Reinvang, Vidar M. Steen, Stephanie Le Hellard, Morten Mattingsdal, Ioanna Ntalla, Vladimir Bencko, Lenka Foretova, Marie Navratilova, Dalila Pinto, Stephen W. Scherer, Harald Aschauer, Laura Carlberg, Alexandra Schosser, Lars Alfredsson, Bo Ding, Leonid Padyukov, Gursharan Kalsi, Marion Roberts, Darren W. Logan, Xavier Estivill, Anke Hinney, Patrick F. Sullivan, David A. Collier, Eleftheria Zeggini and Cynthia M. Bulik

Major Depressive Disorder Working Group of the Psychiatric Genomics Consortium (Major depressive disorder)

Patrick Sullivan, Stephan Ripke, Danielle Posthuma, André G Uitterlinden, Albert Hofman, Stefan Kloiber, Klaus Berger, Bertram Müller-Myhsok, Qingqin Li, Till Andlauer, Marcella Rietschel, Andreas J Forstner, Fabian Streit, Jana Strohmaier, Josef Frank, Stefan Herms, Stephanie Witt, Jens Treutlein, Markus M. Nöthen, Sven Cichon, Franziska Degenhardt, Per Hoffmann, Thomas G. Schulze, Bernhard T Baune, Udo Dannlowski, Tracy Air, Grant Sinnamon, Naomi Wray, Andrew McIntosh, douglas blackwood, Toni-Kim Clarke, Donald MacIntyre, David Porteous, Caroline Hayward, Tonu Esko, Evelin Mihailov, Lili Milani, Andres Metspalu, Hans J Grabe, Henry Völzke, Alexander Teumer, Sandra Van der Auwera, Georg Homuth, Matthias Nauck, Cathryn Lewis, Gerome Breen, Margarita Rivera, Michael Gill, Nick Craddock, John P Rice, Michael Owen, Ole Mors, Anders Børglum, Jakob Grove, Daniel Umbricht, Carsten Horn, Christel Middeldorp, Enda Byrne, Baptiste Couvy-Duchesne, Scott Gordon, Andrew C Heath, Anjali Henders, Ian Hickie, Nicholas Martin, Sarah Medland, Grant Montgomery, Dale Nyholt, Michele Pergadia, Divya Mehta, Martin Preisig, Zoltán Kutalik, Rudolf Uher, Michael O'Donovan, Brenda WJH Penninx, Yuri Milaneschi, Wouter Peyrot, Johannes H Smit, Rick Jansen, Aartjan TF Beekman, Robert A Schoevers, Albert van Hemert, Gerard van Grootheest, Dorret Boomsma, Jouke- Jan Hottenga, Eco de Geus, Erin Dunn, Jordan Smoller, Patrik Magnusson, Nancy Pedersen, Alexander Viktorin, Thomas Werge, Thomas Folkmann Hansen, Sara Paciga, Hualin Xi, Douglas Levinson, James Potash and James A. Knowles

Tourette Syndrome and Obsessive Compulsive Disorder Working Group of the Psychiatric Genomics Consortium (Tourette Syndrome and Obsessive-compulsive disorder)

John Alexander, Paul Arnold, Harald Aschauer, Cristina Barlassina, Cathy Barr, Robert Batterson, Laura Bellodi, Cheston Berlin, Gabriel Bedoya-Berrio, O. Bienvenu,

Donald Black, Michael Bloch, Rianne Blom, Helena Brentani, Lawrence W. Brown, Ruth Bruun, Cathy Budman, Christie Burton, Beatriz Camarena, Carolina Cappi, Julio Cardona-Silgado, Danielle Cath, Maria Cavallini, Keun-Ah Cheon, Barbara J. Coffey, David Conti, Edwin Cook, Nancy Cox, Bernadette Cullen, Daniele Cusi, Sabrina Darrow, Lea Davis, Dieter Deforce, Richard Delorme, Damiaan Denys, Christel Depienne, Eske Derks, Andrea Dietrich, Yves Dion, Shan Dong, Valsamma Eapen, Valsama Eapen, Karin Egberts, Lonneke Elzerman, Patrick Evans, Peter Falkai, Thomas V. Fernandez, Martijn Figee, Nelson Freimer, Odette Fründt, Abby Fyer, Blanca Garcia-Delgar, Helena Garrido, Daniel Geller, Gloria Gerber, Donald L. Gilbert, Fernando Goes, Hans-Jorgen Grabe, Marco Grados, Erica Greenberg, Benjamin Greenberg, Dorothy E. Grice, Edna Grünblatt, Julie Hagstrøm, Gregory Hanna, Andreas Hartmann, Johannes Hebebrand, Tammy Hedderly, Gary A. Heiman, Sian Hemmings, Luis Herrera, Peter Heutink, Isobel Heyman, Matthew Hirschtritt, Pieter J. Hoekstra, Hyun Ju Hong, Ana Hounie, Alden Huang, Chaim Huyser, Laura Ibanez-Gomez, Cornelia Illmann, Michael Jenike, Clare Keenan, James L. Kennedy, Judith Kidd, Kenneth Kidd, Young Key Kim, Young-Shin Kim, Robert A. King, James A. Knowles, Anuar Konkashbaev, Anastasios Konstantinidis, Sodahm Kook, Samuel Kuperman, Nuria Lanzagorta, Marion Leboyer, James Leckman, Phil H Lee, Leonhard Lennertz, Bennett L. Leventhal, Christine Lochner, Thomas Lowe, Andrea G. Ludolph, Gholson Lyon, Fabio Macciardi, Marcos Madruga-Garrido, Brion Maher, Wolfgang Maier, Irene A. Malaty, Paolo Manunta, Athanasios Maras, Carol A. Mathews, Manuel Mattheisen, James McCracken, Lauren McGrath, Nicole McLaughlin, William McMahon, Sandra Mesa Restrepo, Euripedes Miguel, Pablo Mir, Rainald Moessner, Astrid Morer, Kirsten Müller-Vahl, Alexander Münchau, Tara L. Murphy, Dennis Murphy, Benjamin Neale, Gerald Nestadt, Paul S. Nestadt, Humberto Nicolini, Markus Noethen, Erika Nurmi, William Cornejo-Ochoa, Michael S. Okun, Lisa Osiecki, Andrew Pakstis, Peristera Paschou, Michele Pato, Carlos Pato, David Pauls, John Piacentini, Christopher Pittenger, Kerstin J. Plessen, Yehuda Pollak, Danielle Posthuma, Vasily Ramensky, Eliana Mariana Ramos, Steven Rasmussen, Tobias Renner, Victor Reus, Margaret Richter, Mark Riddle, Renata Rizzo, Mary Robertson, Veit Roessner, Maria Rosário, David Rosenberg, Guy Rouleau, Stephan Ruhrmann, Andres Ruiz-Linares, Aline Sampaio, Jack Samuels, Paul Sandor, Jeremiah Scharf, Eun-Young Shin, Yin Shugart, Harvey Singer, Jan Smit, Jordan Smoller, Jungeun Song, Dan Stein, S Evelyn Stewart, Nawei Sun, Jay A. Tischfield, Fotis Tsetsos, Jennifer Tübing, Maurizio Turiel, Ana Valencia Duarte, Homero Vallada, Filip Van Nieuwerburgh, Frank Visscher, Nienke Vulink, Michael Wagner, Susanne Walitza, Sina Wanderer, Ying Wang, Sarah Weatherall, Jens Wendland, Tomasz Wolanczyk, Martin Woods, Yulia Worbe, Jinchuan Xing, Dongmei Yu, Gwyneth Zai, Ivette Zelaya, Yeting Zhang and Samuel H. Zinner

Schizophrenia Working Group of the Psychiatric Genomics Consortium (Schizophrenia)
Rolf Adolfsson, Ingrid Agartz, Ole Andreassen, Martin Begemann, Sarah Bergen, Donald Black, Douglas Blackwood, Anders Børglum, Elvira Bramon, Richard Bruggeman, Nancy Buccola, Brendan Bulik-Sullivan, Joseph Buxbaum, William Byerley, Wiepke Cahn, Murray Cairns, Dominique Campion, Rita Cantor, Vaughan Carr, Raymond Chan, Ronald Chen, Wei Cheng, Eric Cheung, Siow Chong, Sven Cichon,

Robert Cloninger, David Cohen, David Collier, Paul Cormican, Aiden Corvin, Nick Craddock, Benedicto Crespo-Facorro, James Crowley, David Curtis, Mark Daly, Michael Davidson, Franziska Degenhardt, Jurgen Del Favero, Lynn DeLisi, Ditte Demontis, Timothy Dinan, Srdjan Djurovic, Enrico Domenici, Gary Donohoe, Elodie Drapeau, Jubao Duan, Hannelore Ehrenreich, Johan Eriksson, Valentina Escott-Price, Tõnu Esko, Ayman Fanous, Kai-How Farh, Josef Frank, Lude Franke, Robert Freedman, Nelson Freimer, Joseph Friedman, Menachem Fromer, Pablo Gejman, Elliot Gershon, Ina Giegling, Michael Gill, Paola Giusti-Rodríguez, Stephanie Godard, Lieuwe Haan, Christian Hammer, Marian Hamshere, Thomas Hansen, Vahram Haroutunian, Annette Hartmann, Frans Henskens, Stefan Herms, Per Hoffmann, Andrea Hofman, Peter Holmans, David Hougaard, Hailiang Huang, Christina Hultman, Assen Jablensky, Inge Joa, Erik Jönsson, Antonio Julià, René Kahn, Luba Kalaydjieva, Sena Karachanak-Yankova, Brian Kelly, Kenneth Kendler, James Kennedy, Andrey Khrunin, George Kirov, Janis Klovins, Jo Knight, James A. Knowles, Bettina Konte, Vaidutis Kucinskas, Claudine Laurent, Phil H Lee, Hong Lee, Jimmy Lee Chee Keong, Bernard Lerer, Douglas Levinson, Miaoxin Li, Tao Li, Qingqin Li, Svetlana Limborska, Jianjun Liu, Carmel Loughland, Jouko Lönnqvist, Milan Macek, Patrik Magnusson, Brion Maher, Wolfgang Maier, Sara Marsal, Manuel Mattheisen, Morten Mattingsdal, Colm McDonald, Andrew McIntosh, Andrew McQuillin, Sandra Meier, Ingrid Melle, Andres Metspalu, Lili Milani, Derek Morris, Ole Mors, Preben Mortensen, Bryan Mowry, Bertram Müller-Myhsok, Kieran Murphy, Robin Murray, Benjamin Neale, Igor Nenadic, Gerald Nestadt, Annelie Nordin, Markus M. Nöthen, Eadbhard O'Callaghan, Michael O'Donovan, Sang-Yun Oh, Roel Ophoff, Jim Os, Michael Owen, Aarno Palotie, Christos Pantelis, Sergi Papiol, Michele Pato, Carlos Pato, Psychosis Endophenotypes International Consortium, Tracey Petryshen, Jonathan Pimm, Danielle Posthuma, Alkes Price, Shaun Purcell, Digby Quested, Abraham Reichenberg, Alexander Richards, Marcella Rietschel, Brien Riley, Stephan Ripke, Joshua Roffman, Panos Roussos, Douglas Ruderfer, Dan Rujescu, Veikko Salomaa, Alan Sanders, Ulrich Schall, Sibylle Schwab, Rodney Scott, Pak Sham, Jeremy Silverman, Kang Sim, Pamela Sklar, Jordan Smoller, Hon-Cheong So, David Clair, Eli Stahl, Elisabeth Stögmann, Jana Strohmaier, Scott Stroup, Mythily Subramaniam, Patrick Sullivan, Jaana Suvisaari, Jin Szatkiewicz, Srinivas Thirumalai, Draga Toncheva, Sarah Tosato, John Waddington, James Walters, Dai Wang, Qiang Wang, Bradley Webb, Mark Weiser, Thomas Werge, Dieter Wildenauer, Nigel Williams, Stephanie Witt, Emily Wong, Naomi Wray, Wellcome Trust Case-Control Consortium 2, Hualin Xi, Clement Zai and Fritz Zimprich

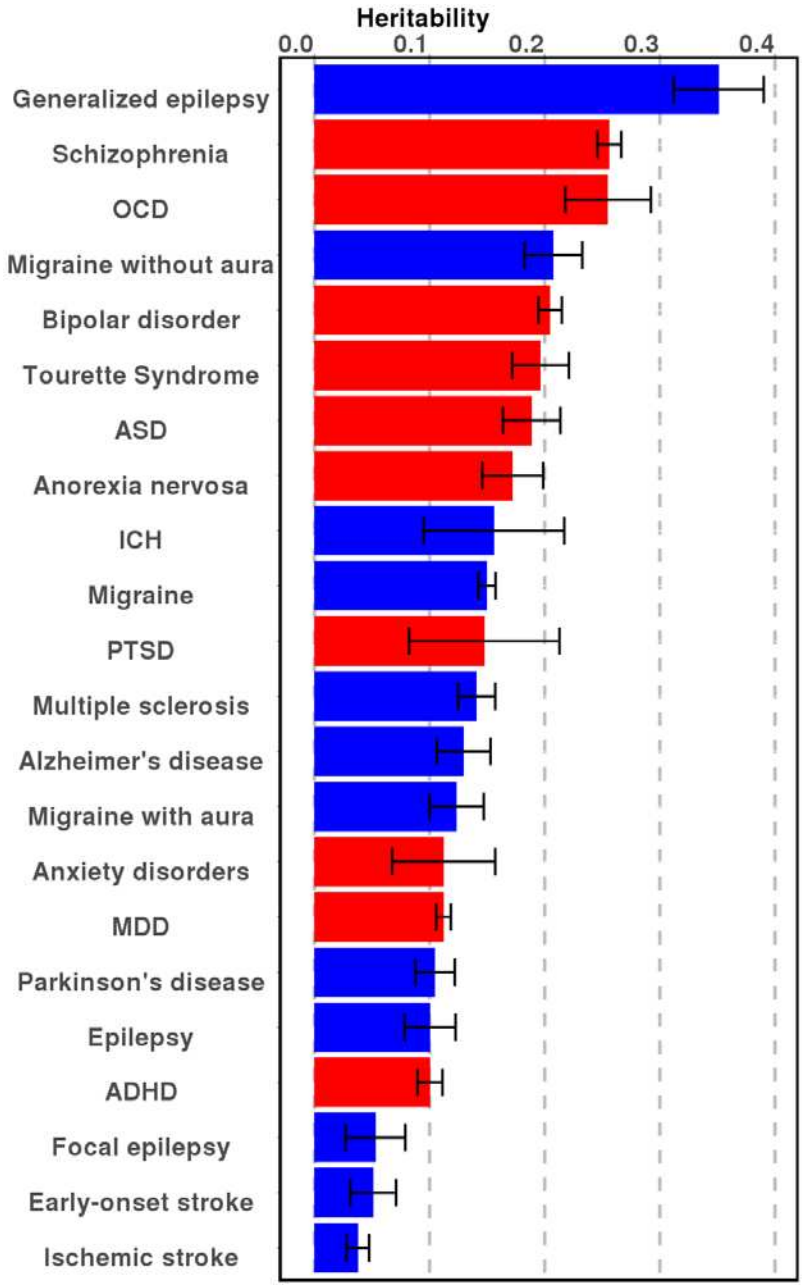


Fig. S1A. Heritability estimates for brain disorders

Red bars denote psychiatric disorders, while blue bars denote neurological disorders. ADHD – attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. Error bars show one standard error.

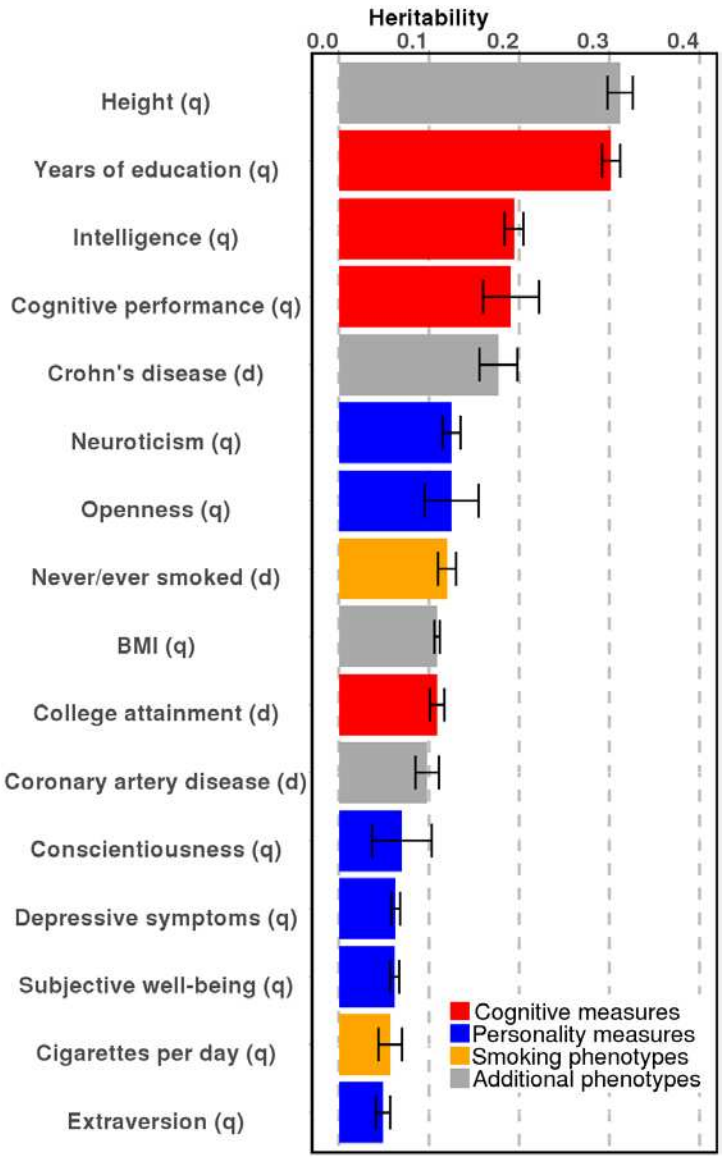


Fig. S1B. Heritability estimates for quantitative and additional phenotypes

BMI – body-mass index. Heritabilities are reported on the observed scale for quantitative phenotypes (q) and liability scale for dichotomous phenotypes (d). Error bars show one standard error.

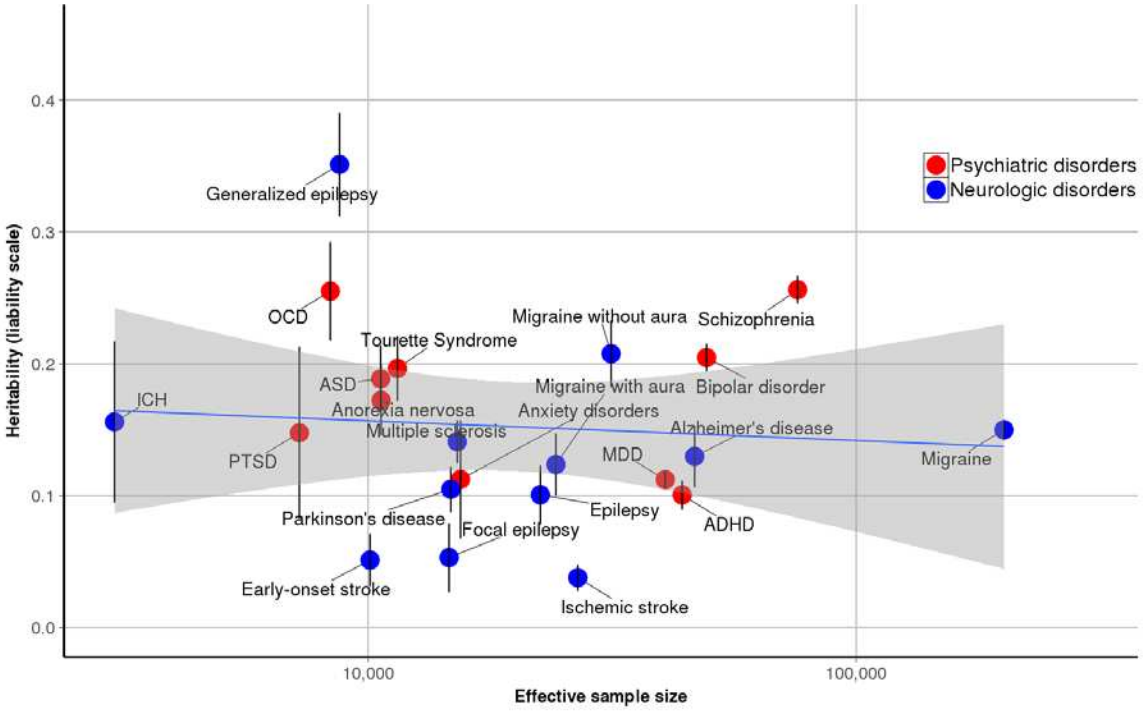


Fig. S1C. Heritability and effective sample size

ADHD – attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. Shaded area shows 95% confidence interval. Error bars show one standard error.

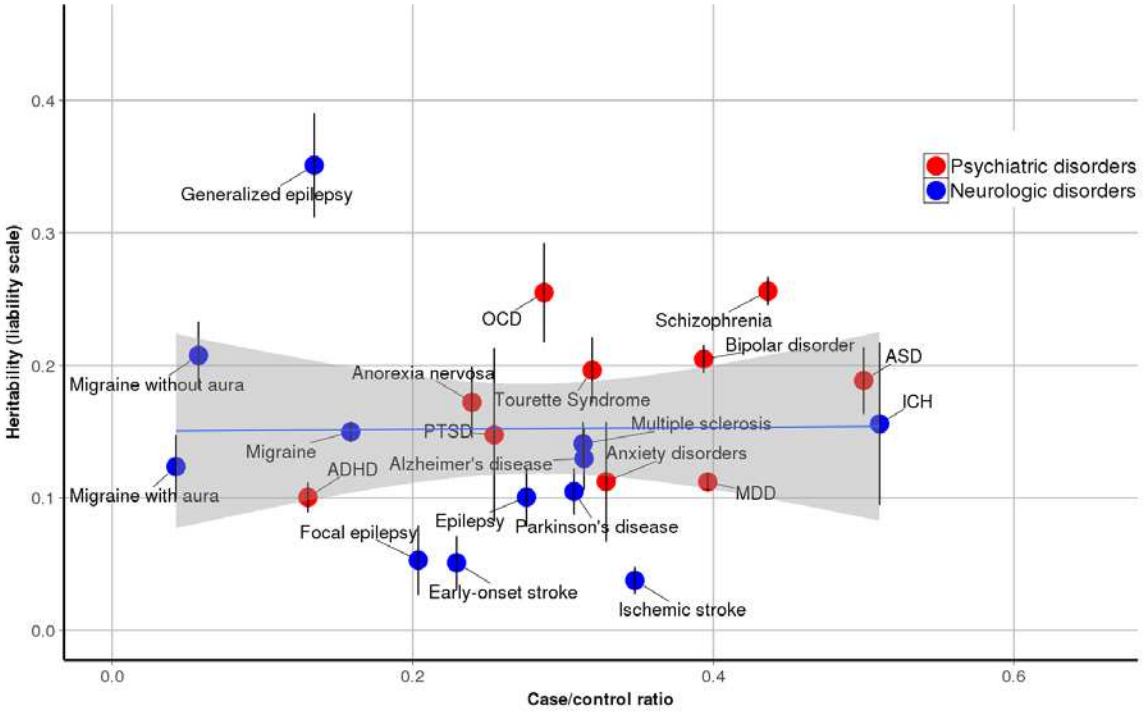


Fig. S1D. Heritability and case/control ratio

ADHD – attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. Shaded area shows 95% confidence interval. Error bars show one standard error.

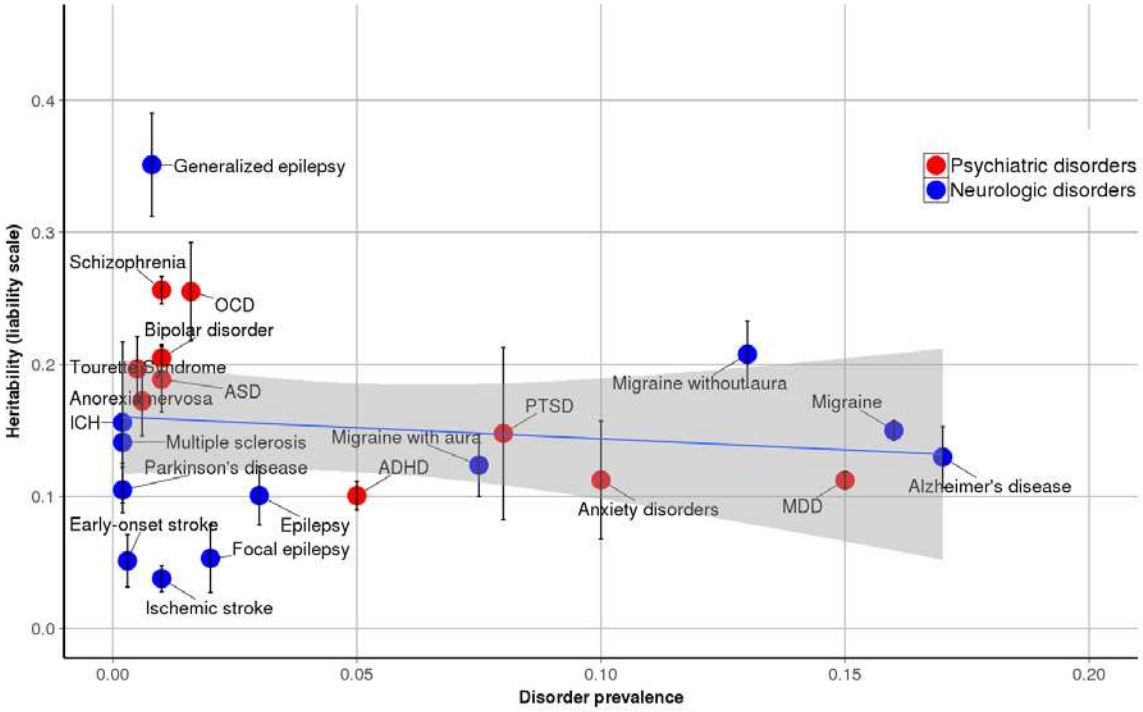


Fig. S1E. Heritability and disorder prevalence

ADHD – attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. Shaded area shows 95% confidence interval. Error bars show one standard error.

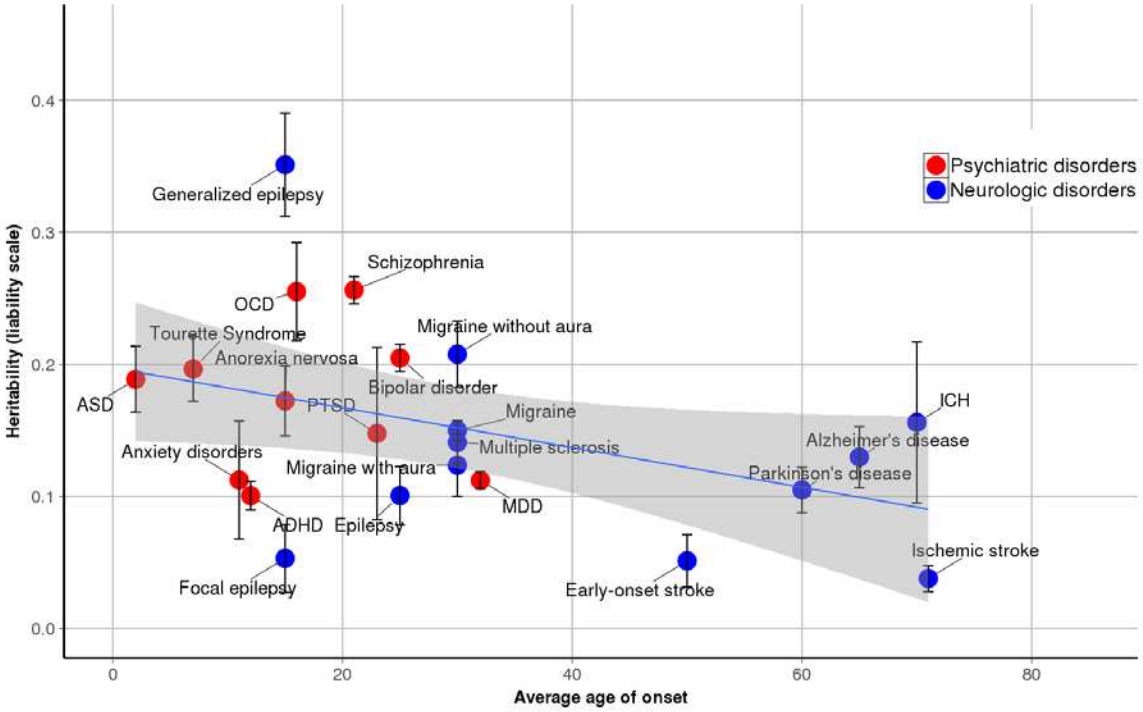
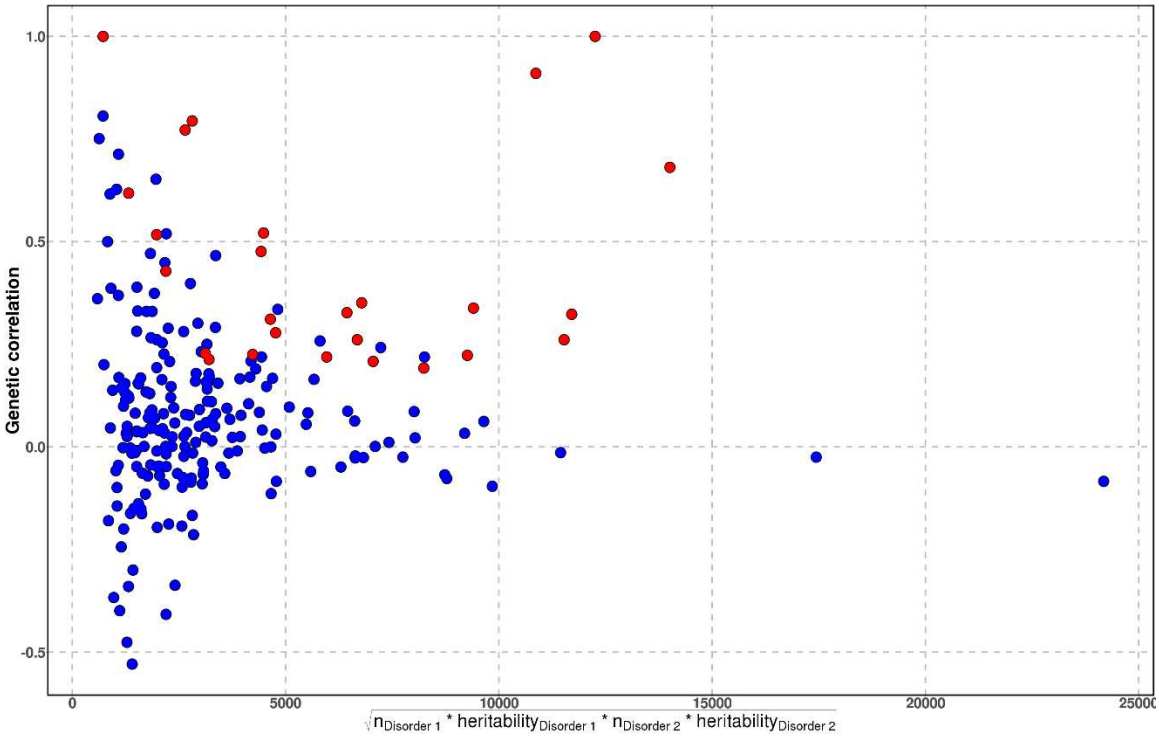


Fig. S1F. Heritability and average age of onset for the disorder.

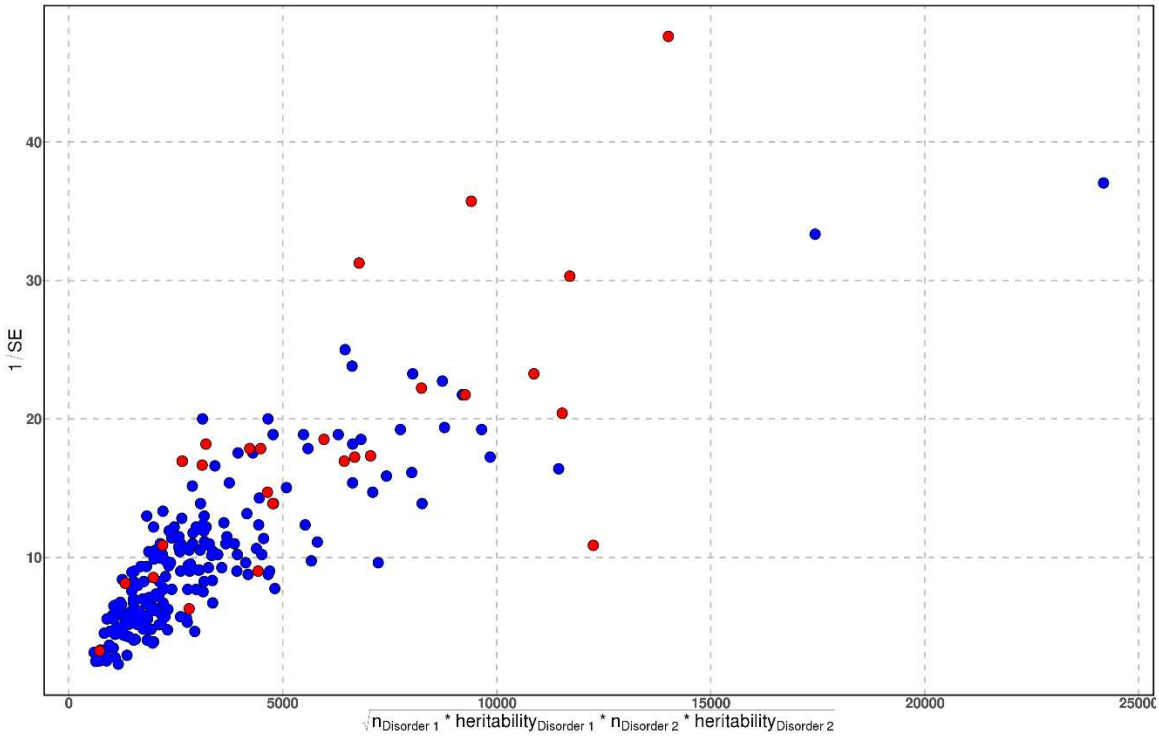
ADHD – attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. Shaded area shows 95% confidence interval. Error bars show one standard error.

Fig. S2A. Genetic correlations against power to detect heritability



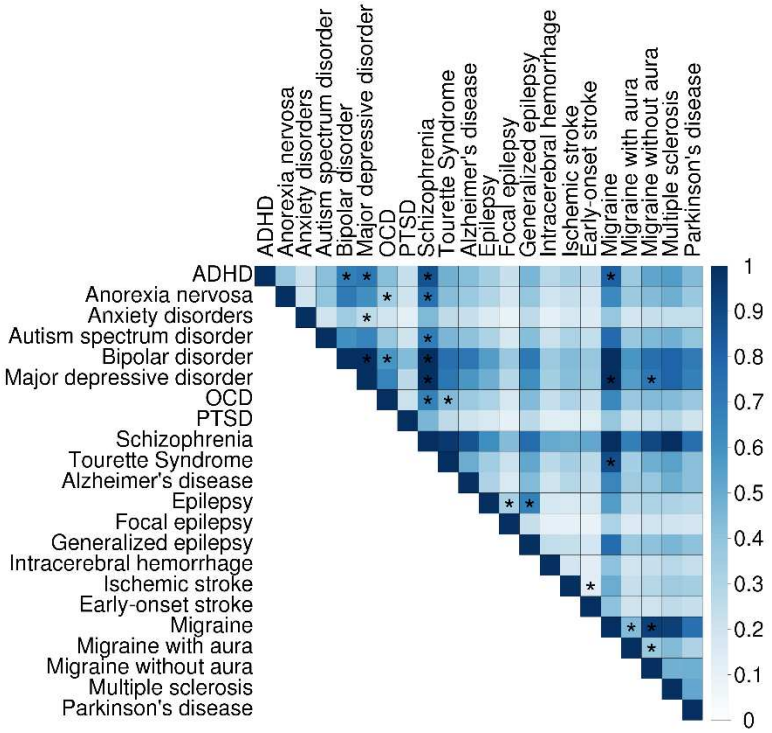
Red points show significant correlations among all disorder-disorder pairs. Two outlier values over 1 (see Table S7A) have been reduced to 1. The points close or equal to $r_g = 1$ are pairs of a top-level disorder with a subtype of the same disorder, where high correlation is expected, ie. all migraine and migraine with aura.

Fig. S2B. Inverses of standard errors against power to detect heritability



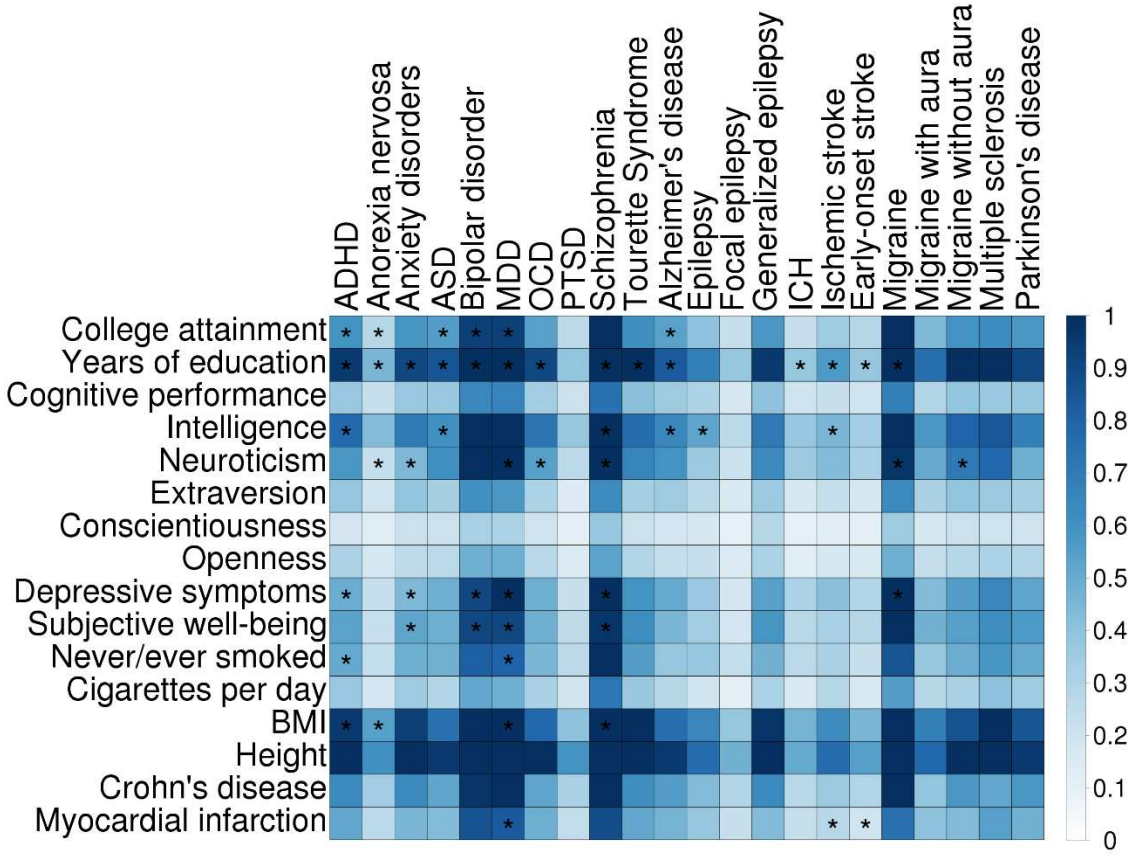
Red points show significant correlations among all disorder-disorder pairs. SE – standard error.

Fig. S2C. Matrix of standard errors for the genetic correlations for disorder-disorder pairs.



Plotted values indicate 1/standard error * 1/25 (1/25 chosen for scaling convenience); darker shades indicate tests with more power. Six outlier values over 1 (see Table S7A) have been reduced to 1. Asterisks highlight results which are significant after Bonferroni correction. ADHD - attention deficit hyperactivity disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder.

Fig. S2D. Matrix of standard errors for the genetic correlations for disorder-phenotype pairs.



Plotted values indicate 1/standard error * 1/25 (1/25 chosen for scaling convenience); darker shades indicate tests with more power. 39 outlier values over 1 (see Table S7B) have been reduced to 1. Asterisks highlight results which are significant after Bonferroni correction. ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; BMI – body-mass index; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder.

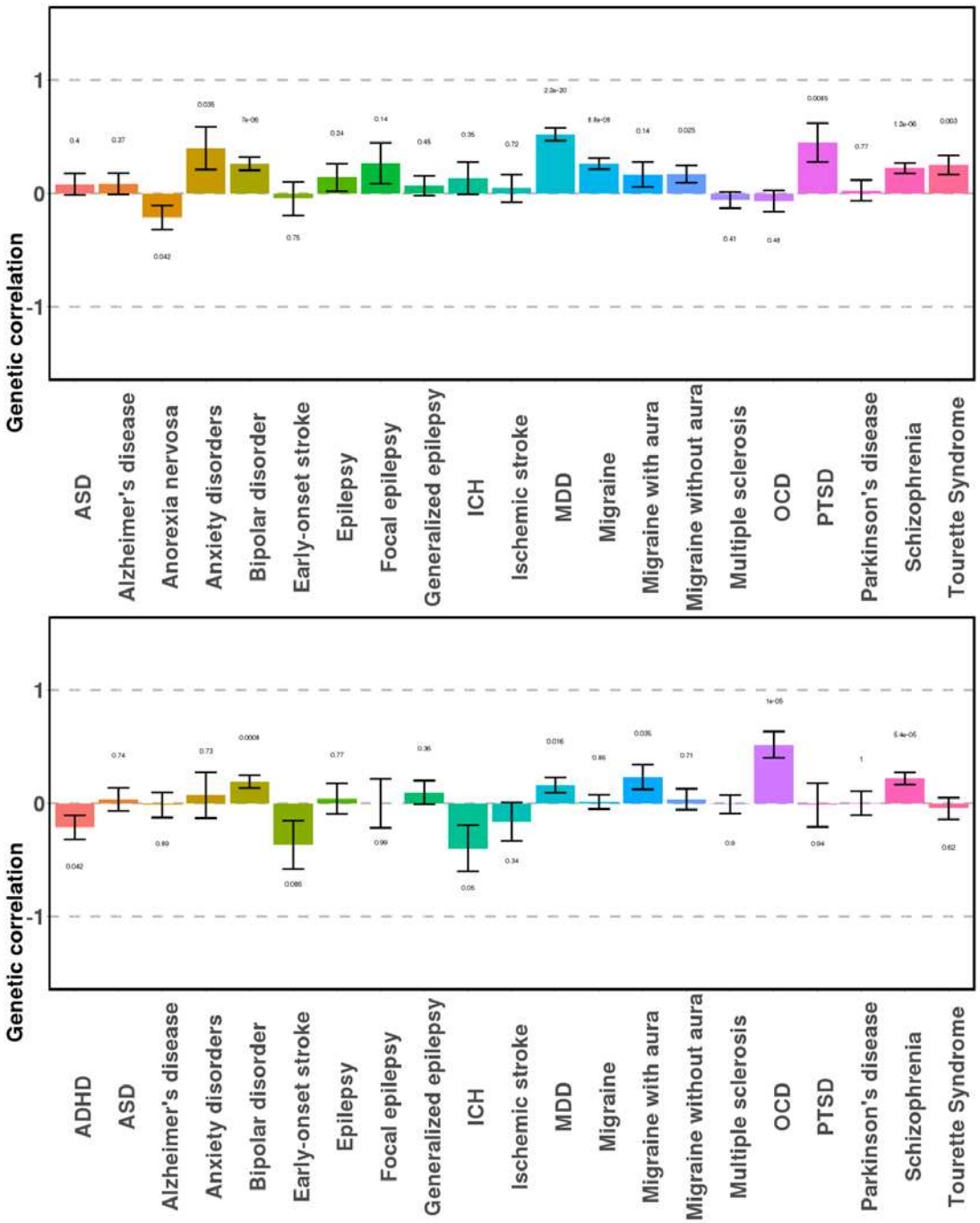


Fig. S3A and B. Genetic correlations for attention-deficit hyperactivity disorder (top) and anorexia nervosa (bottom).

ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. P-values for correlation are shown at the end of each bar. Error bars show one standard error.

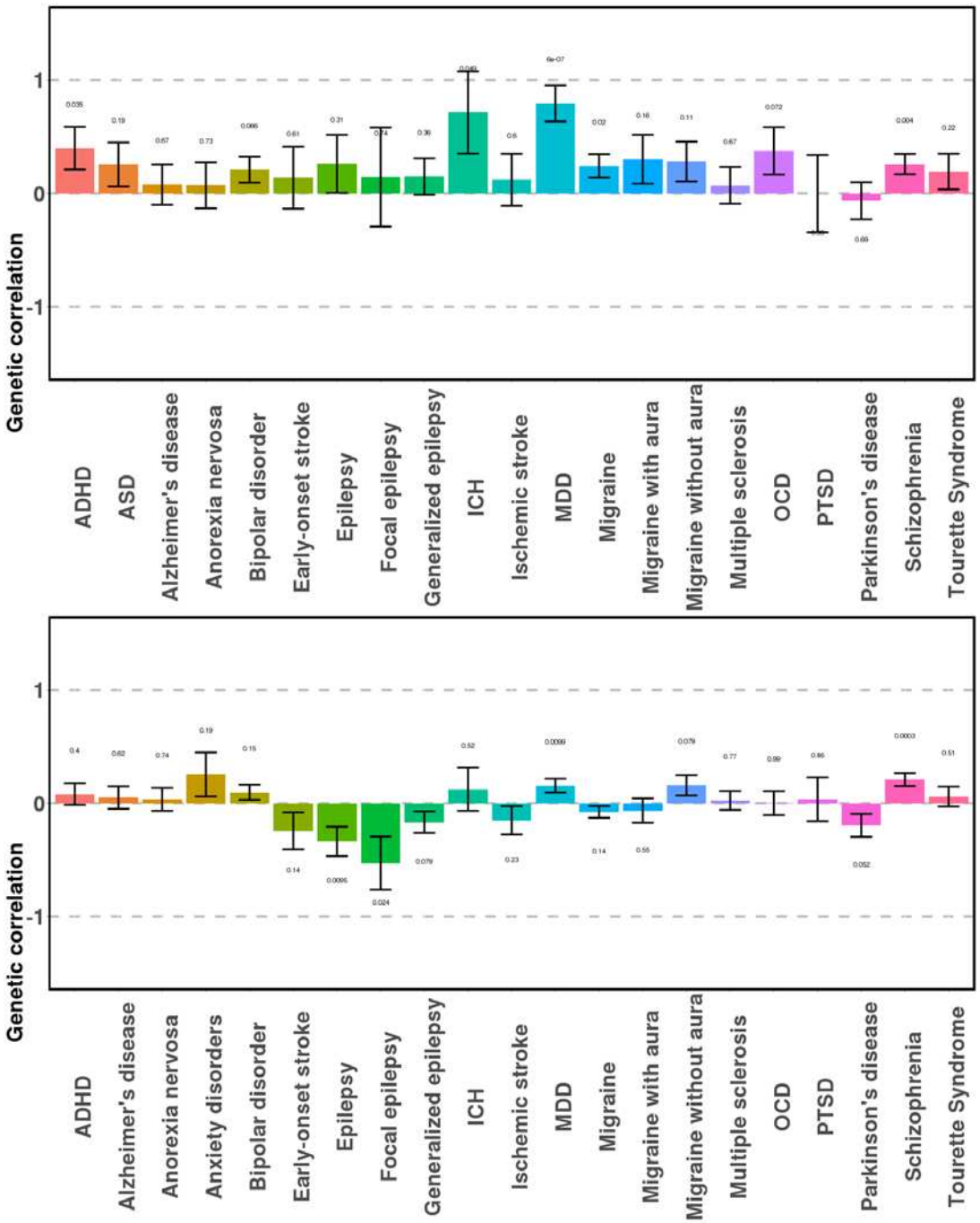


Fig. S3C and D. Genetic correlations for anxiety disorders (top) and autism spectrum disorder (bottom).

ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. P-values for correlation are shown at the end of each bar. Error bars show one standard error.

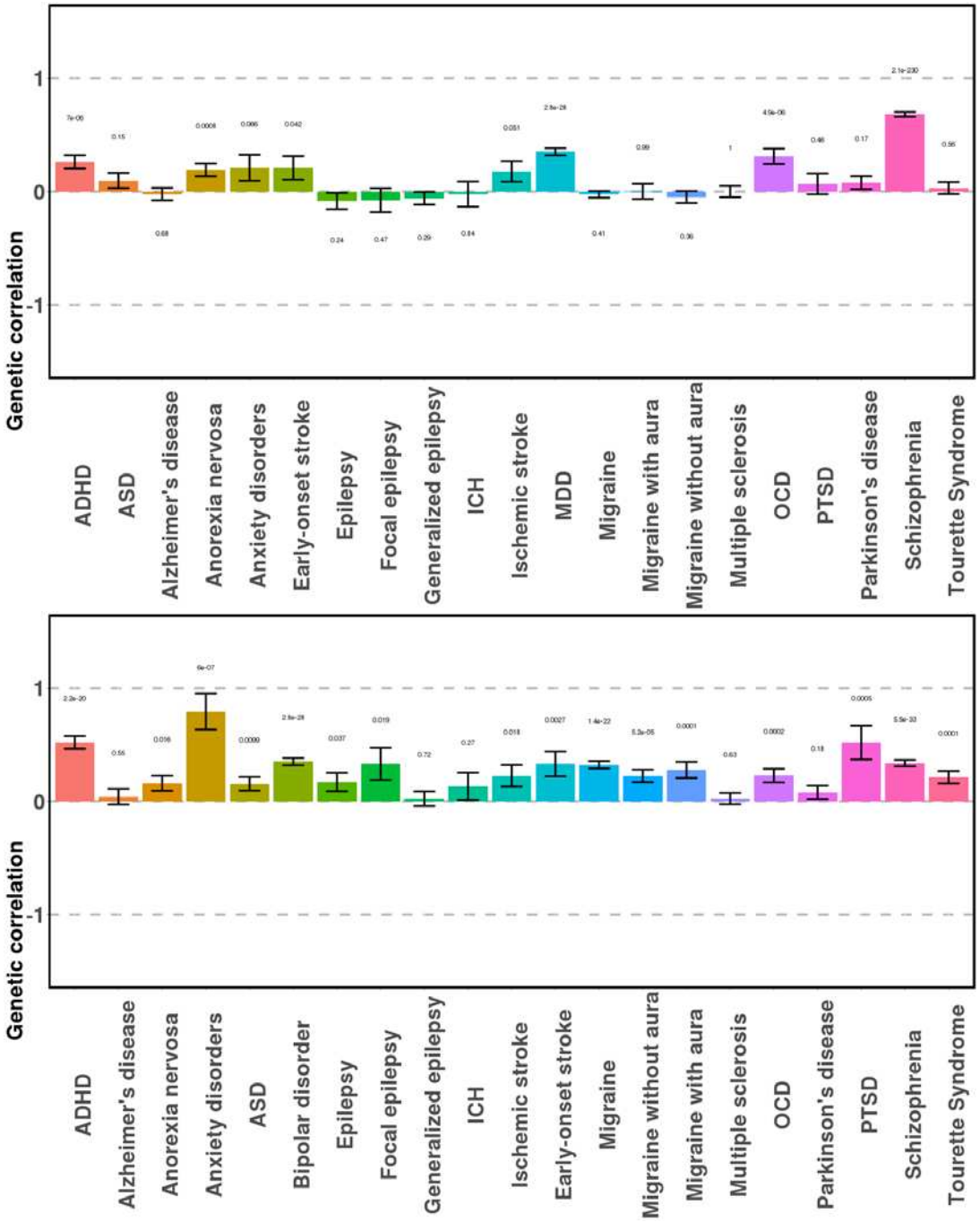


Fig. S3E and F. Genetic correlations for bipolar disorder (top) and major depressive disorder (bottom).

ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. P-values for correlation are shown at the end of each bar. Error bars show one standard error.

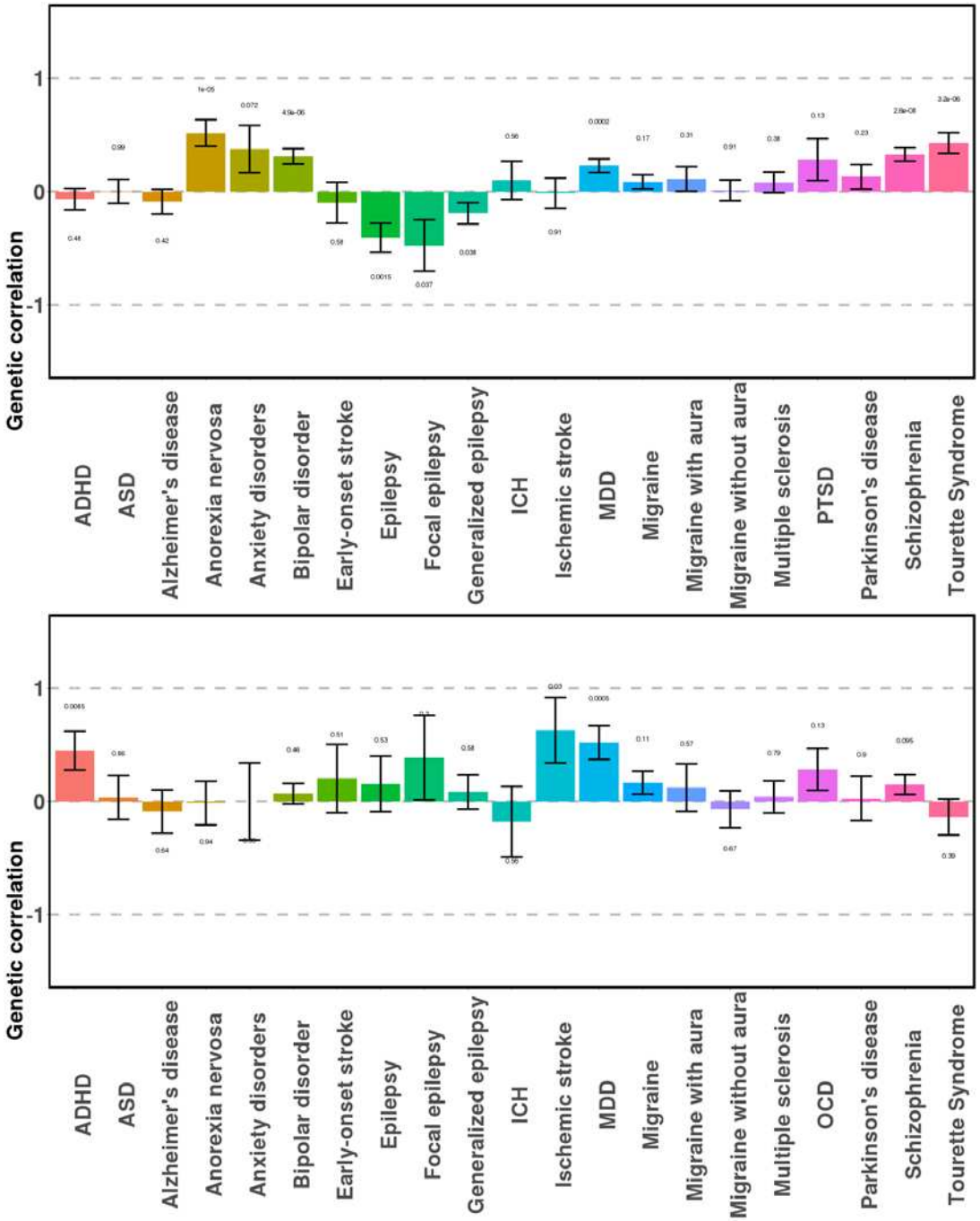


Fig. S3G and H. Genetic correlations for obsessive-compulsive disorder (top) and post-traumatic stress disorder (bottom).

ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. P-values for correlation are shown at the end of each bar. Error bars show one standard error.

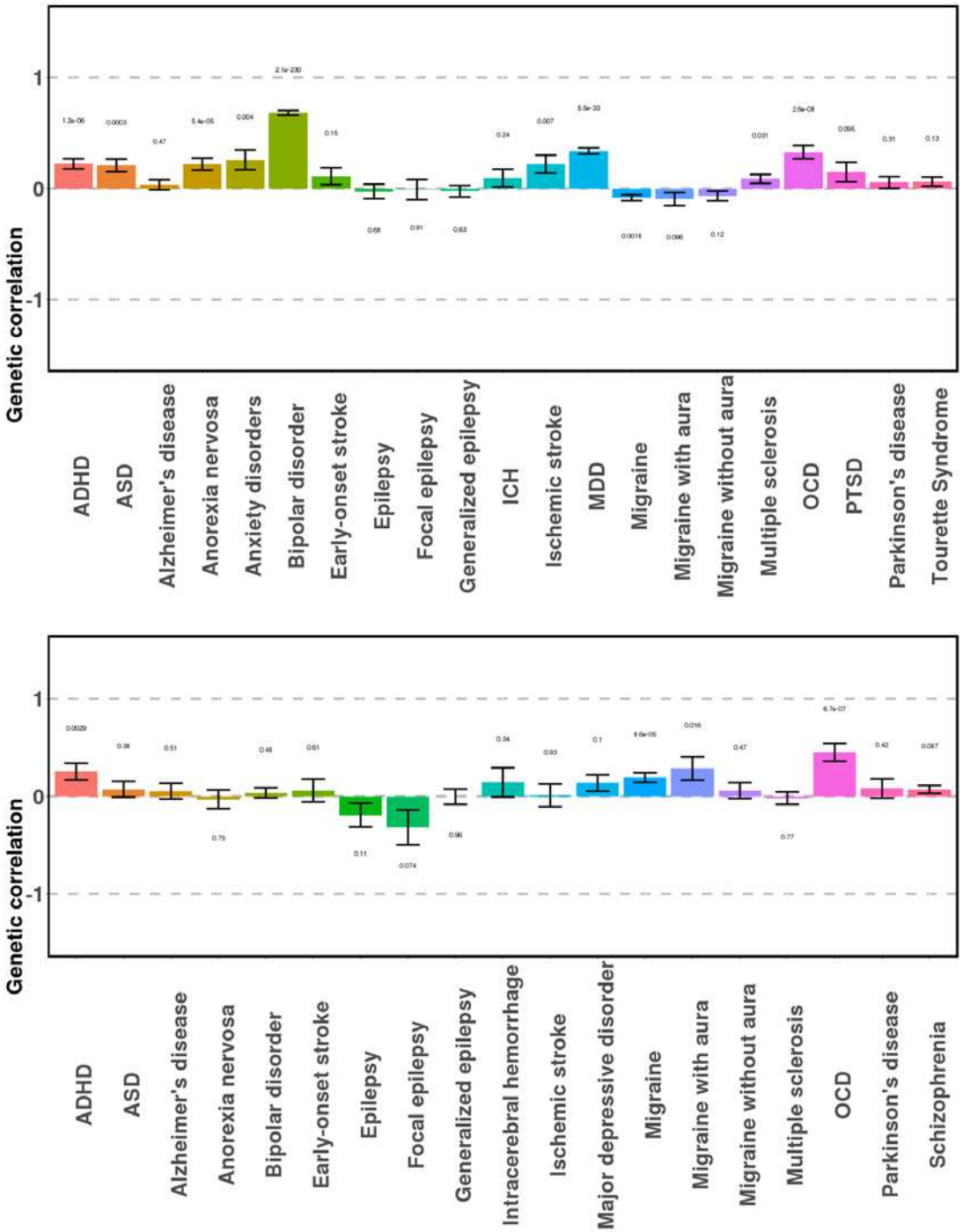


Fig. S3I and J. Genetic correlations for schizophrenia (top) and Tourette Syndrome (bottom).

ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. P-values for correlation are shown at the end of each bar. Error bars show one standard error.

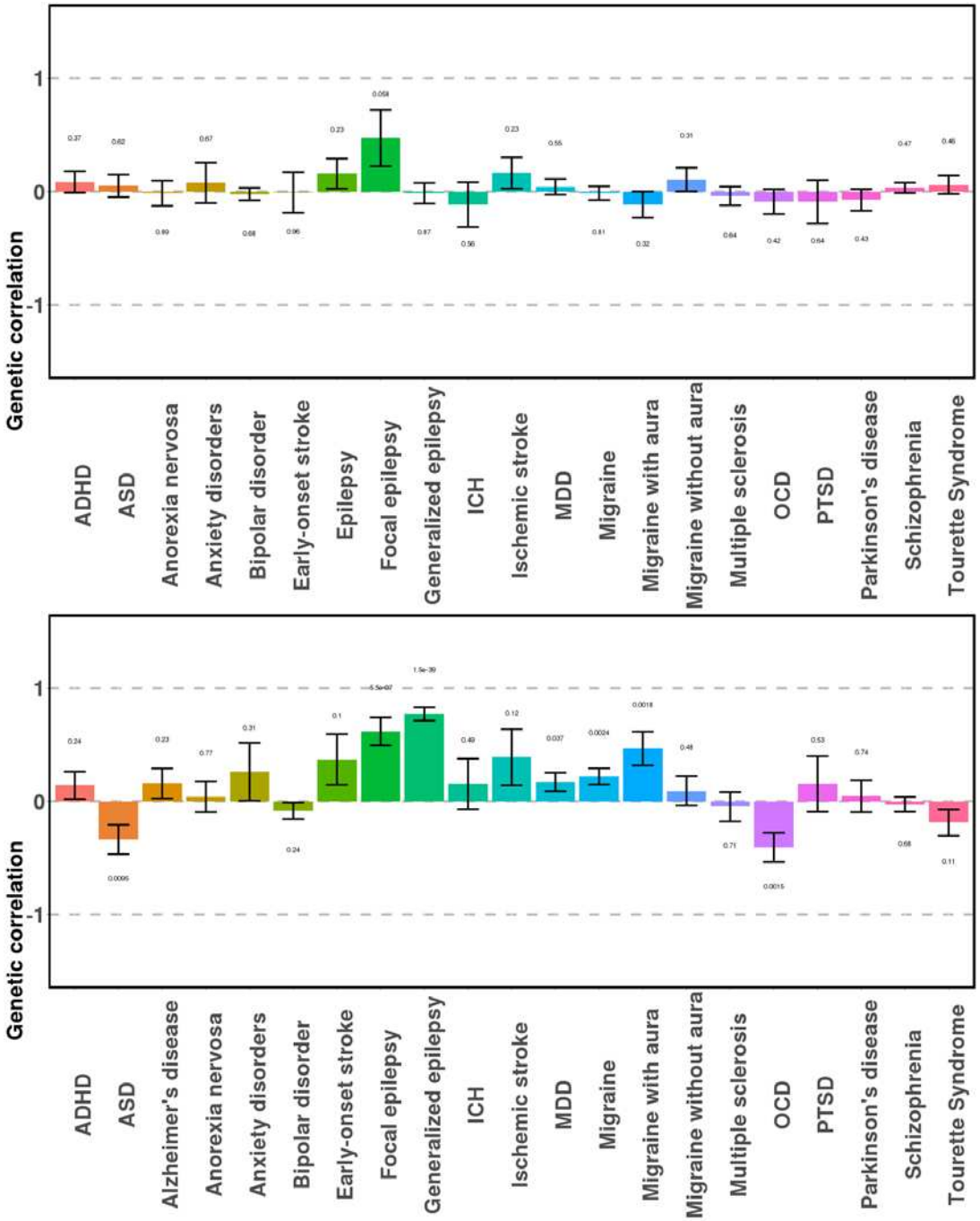


Fig. S4A and B. Genetic correlations for Alzheimer's disease (top) and epilepsy (bottom).

ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. P-values for correlation are shown at the end of each bar. Error bars show one standard error.

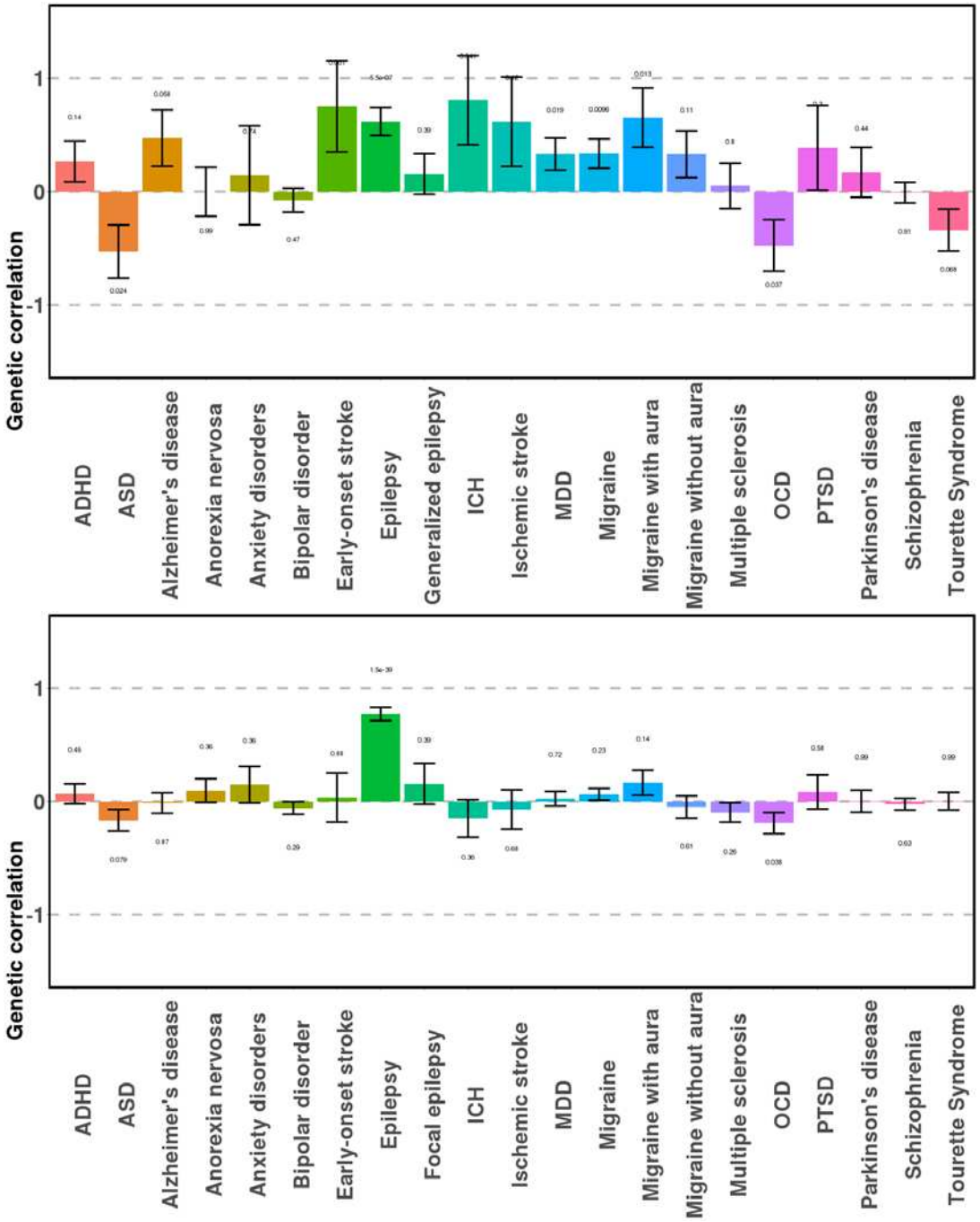


Fig. S4C and D. Genetic correlations for focal epilepsy (top) and generalized epilepsy (bottom).

ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. P-values for correlation are shown at the end of each bar. Error bars show one standard error.

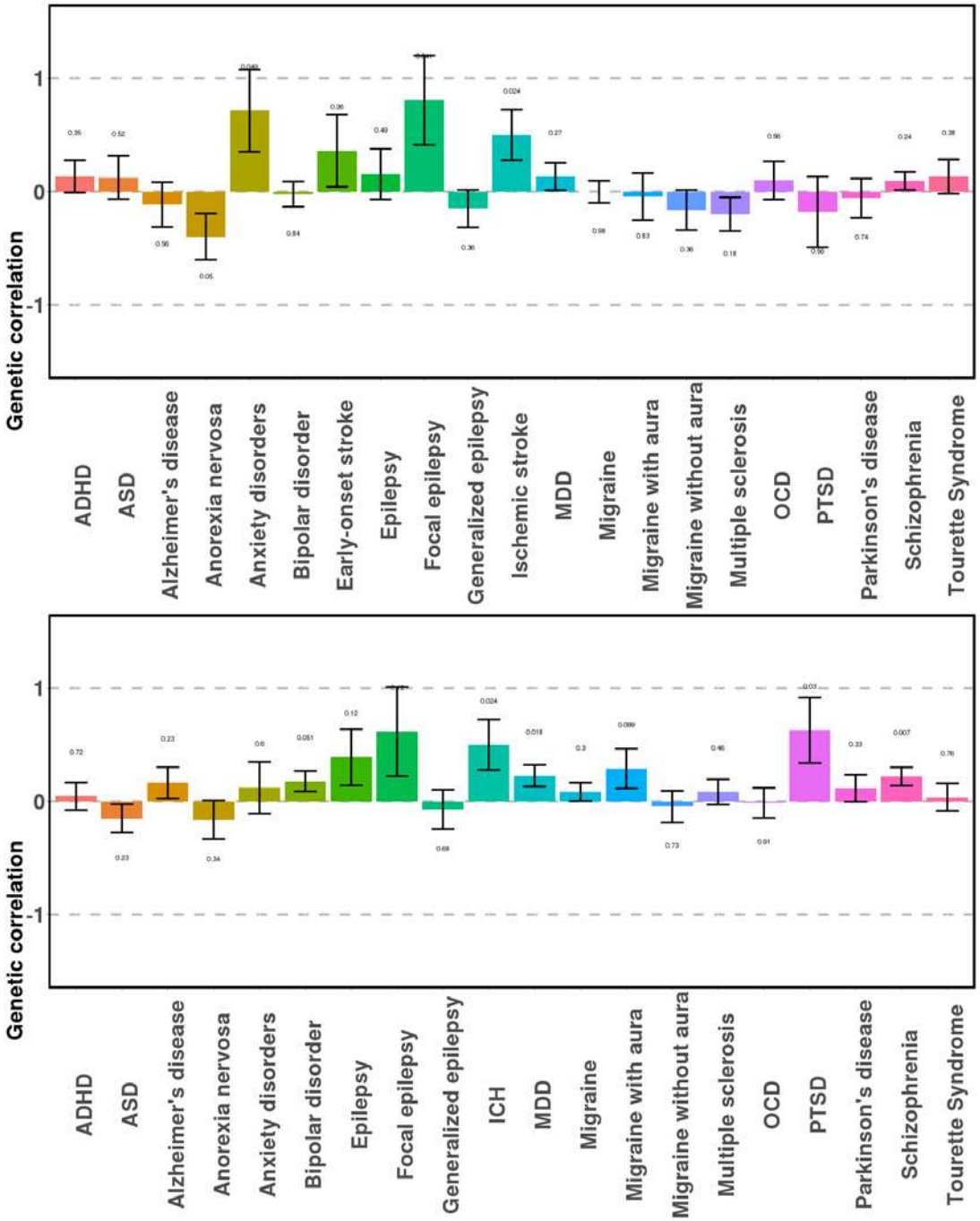


Fig. S4E and F. Genetic correlations for intracerebral hemorrhage (top) and ischemic stroke (bottom).

ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. P-values for correlation are shown at the end of each bar. Error bars show one standard error.

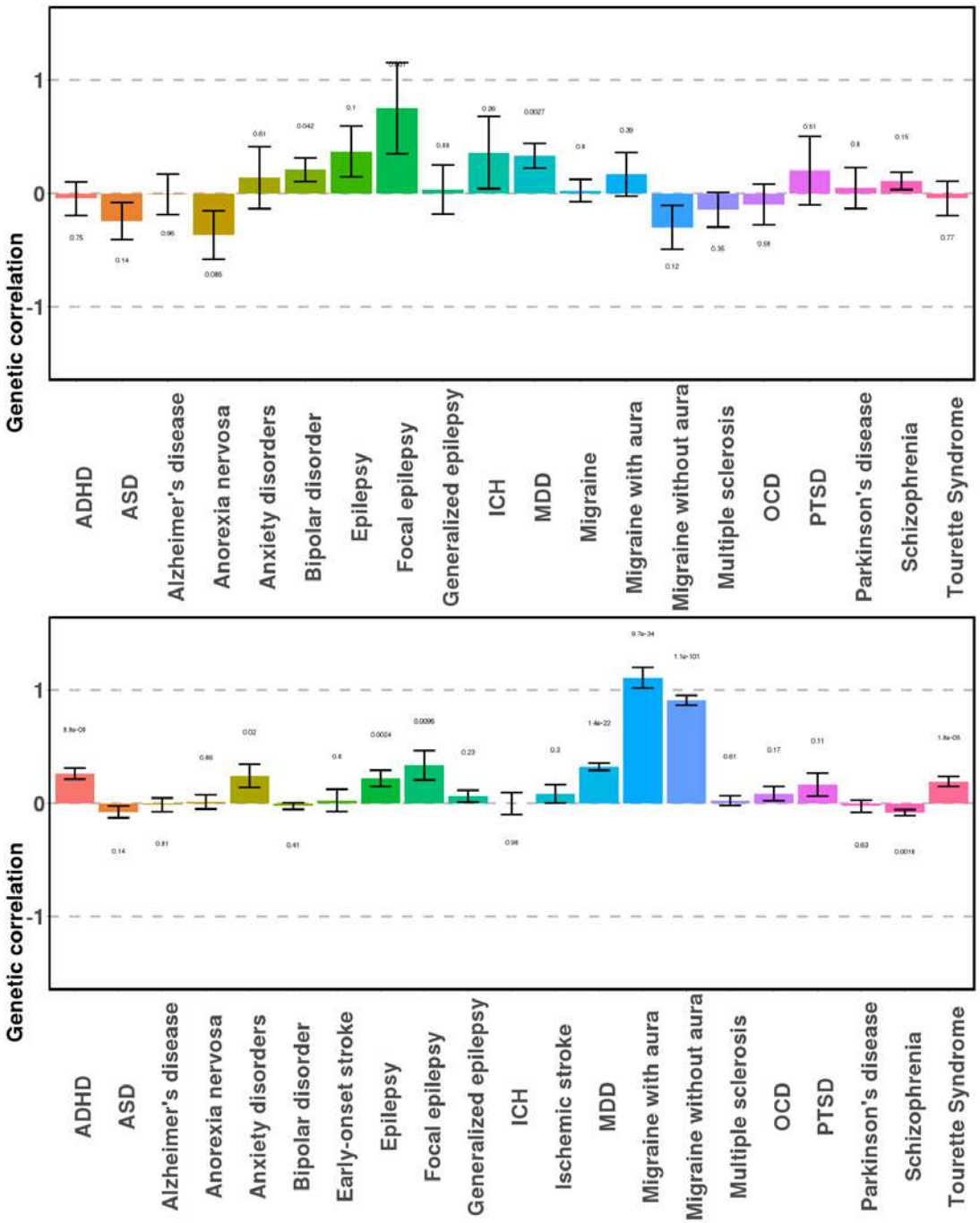


Fig. S4G and H. Genetic correlations for early-onset stroke (top) and migraine (bottom).

ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. P-values for correlation are shown at the end of each bar. Error bars show one standard error.

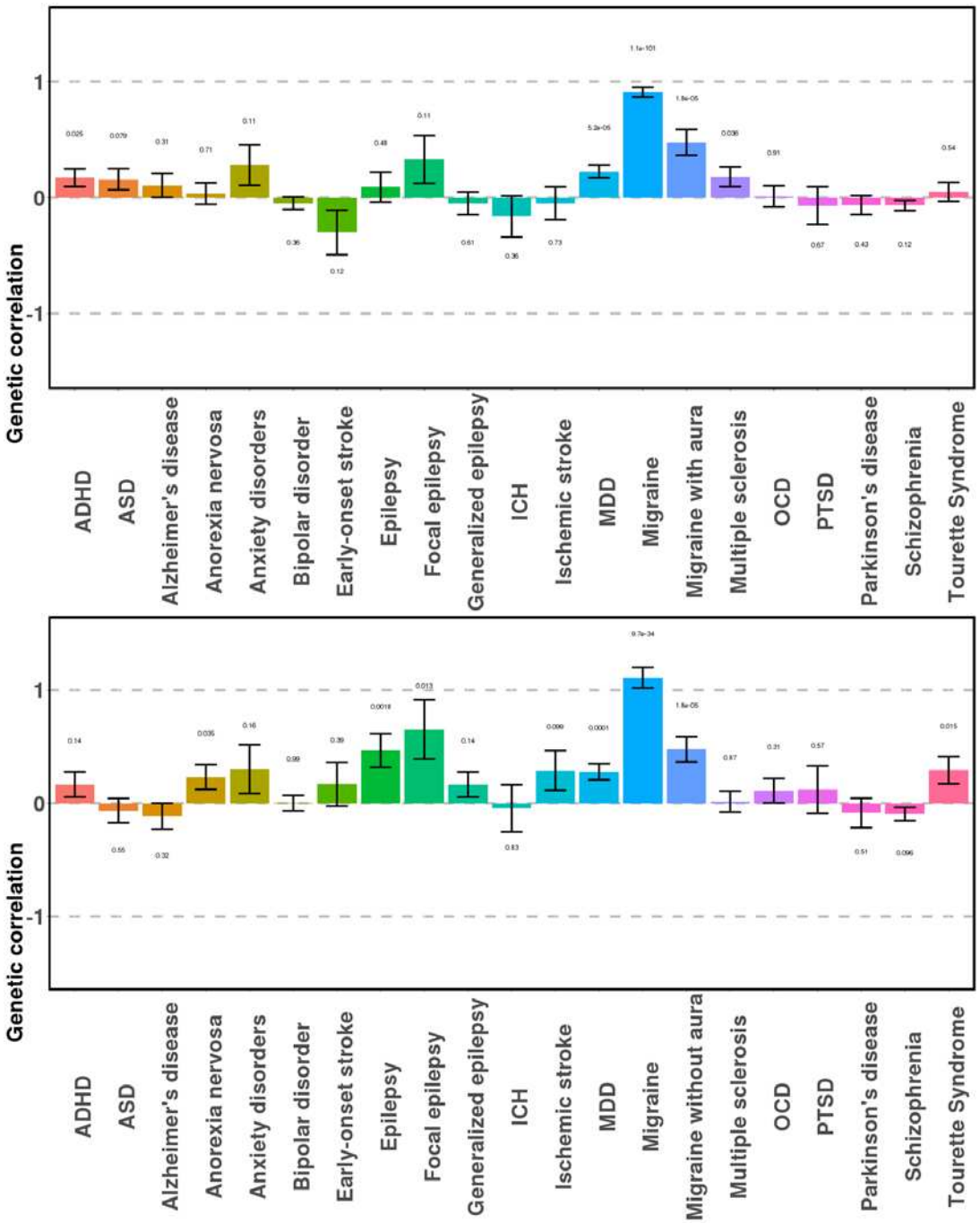


Fig. S4I and J. Genetic correlations for migraine without aura (top) and migraine with aura (bottom).

ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. P-values for correlation are shown at the end of each bar. Error bars show one standard error.

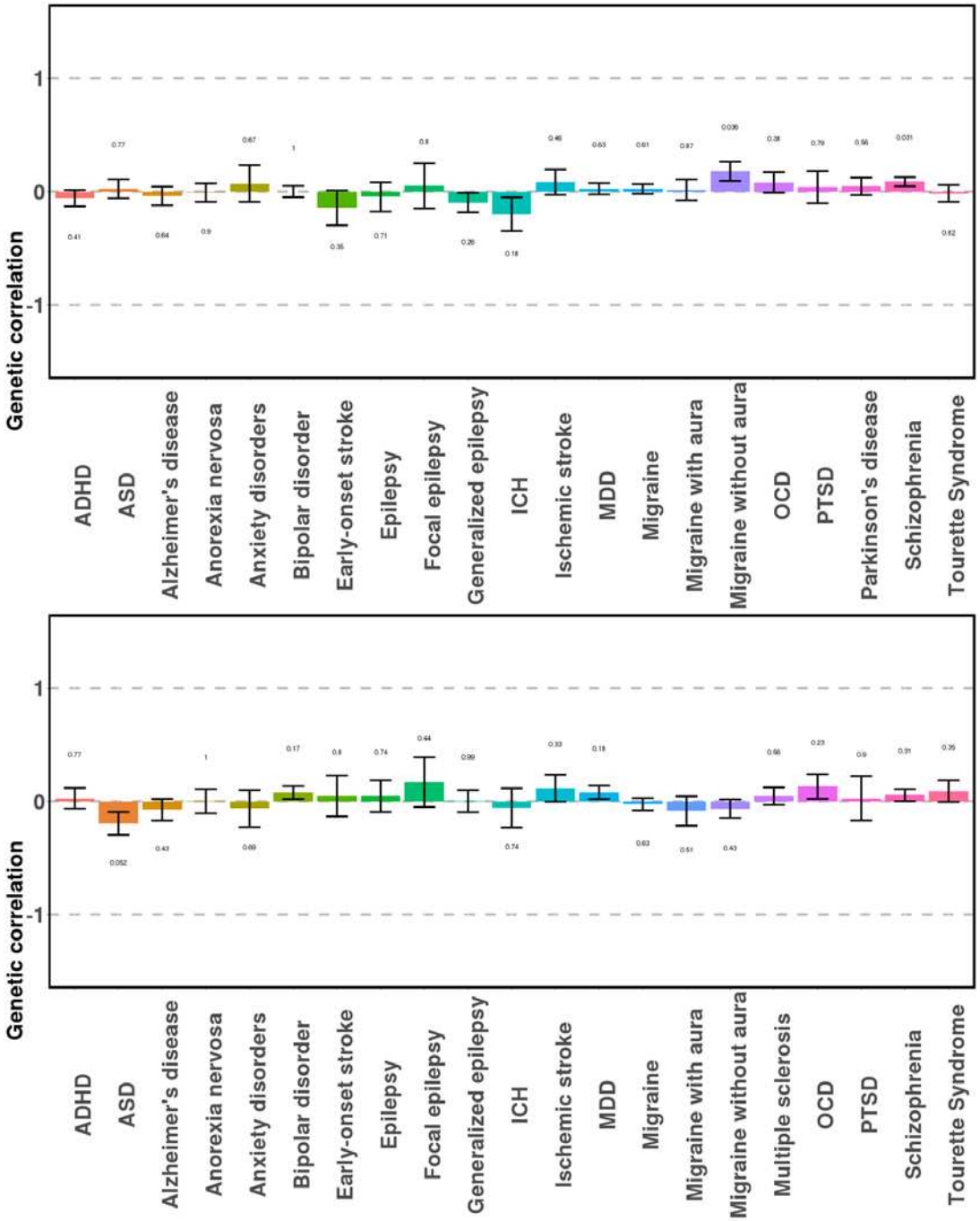


Fig. S4K and L. Genetic correlations for multiple sclerosis (top) and Parkinson's disease (bottom).

ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. P-values for correlation are shown at the end of each bar. Error bars show one standard error.

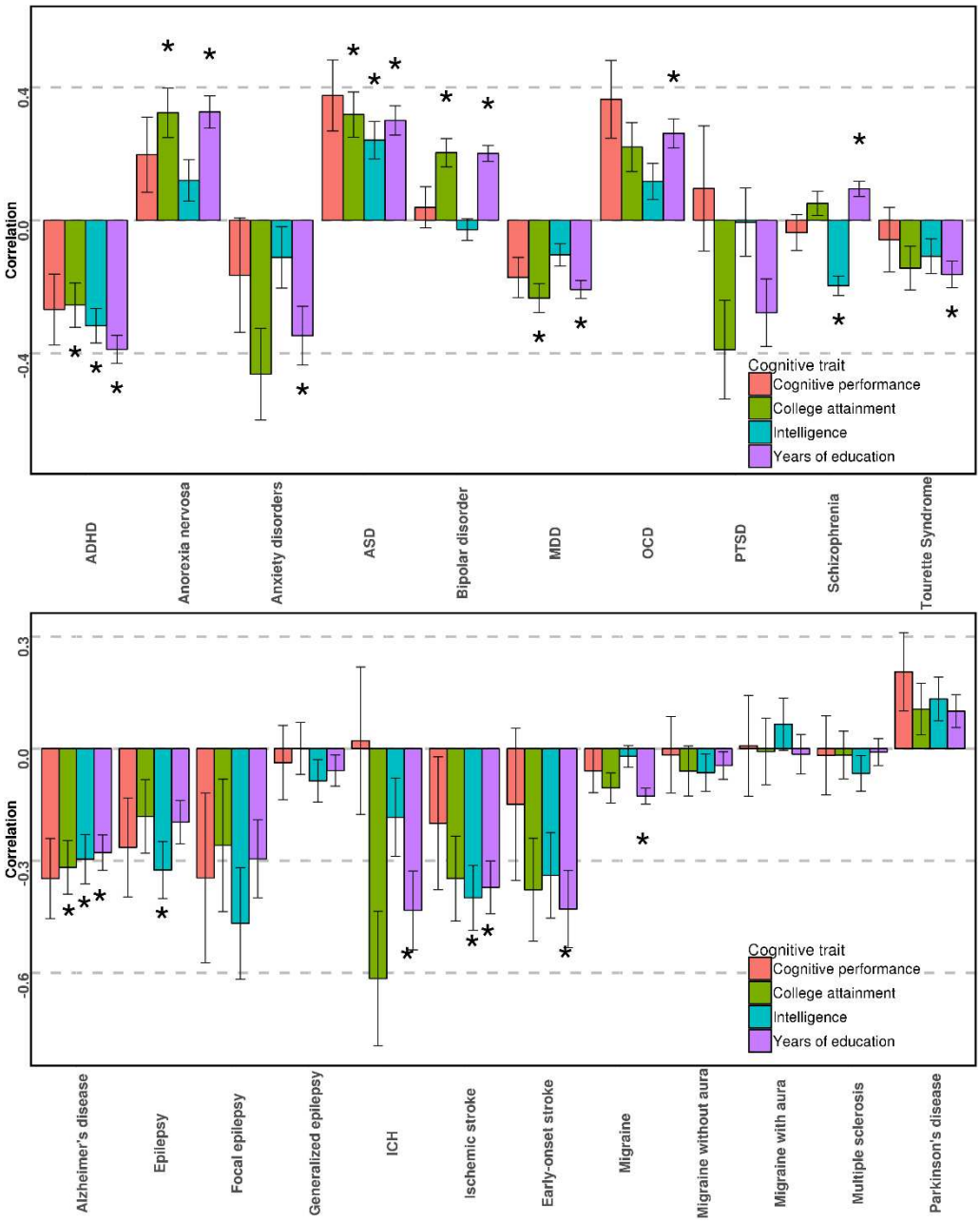


Fig. S5A and B. Genetic correlations for psychiatric and neurological disorders against cognitive measures.

Asterisks highlight results which are significant after Bonferroni correction. ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder; ICH – intracerebral hemorrhage. Dotted line divides the psychiatric phenotypes from the neurological phenotypes. Error bars show one standard error.

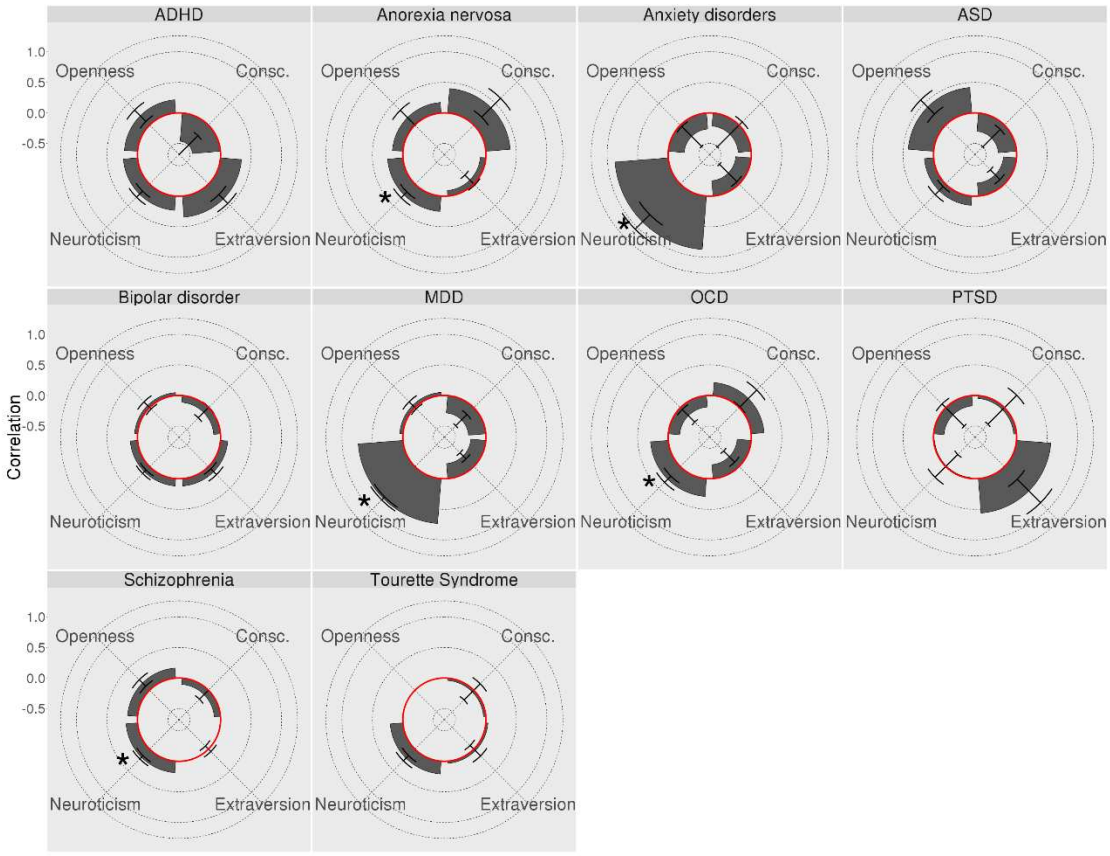


Fig. S6A. Genetic correlations for psychiatric disorders and four personality axes.
Grey sectors denote the extent of genetic correlation between each brain disorder and the four personality axes. Red line denotes zero correlation, with positive correlations on the outside and negative correlations on the inside. Error bars show one standard error. Asterisks highlight results which are significant after Bonferroni correction. Consc. – Conscientiousness; ADHD - attention deficit hyperactivity disorder; ASD – autism spectrum disorder; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder.

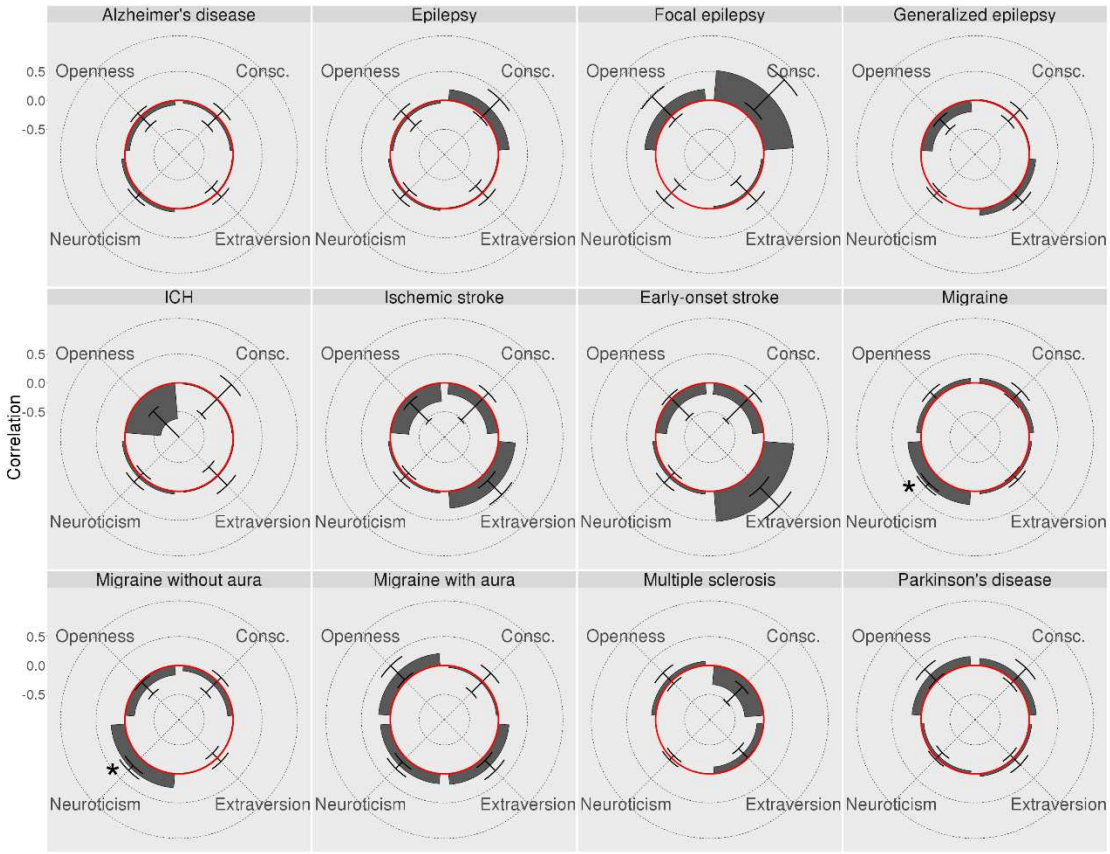


Fig. S6B. Genetic correlations for neurological disorders and four personality axes. Grey bars denote the extent of genetic correlation between each brain disorder and the four personality axes. Red line denotes zero correlation, with positive correlations on the outside and negative correlations on the inside. Error bars show one standard error. Asterisks highlight results which are significant after Bonferroni correction. Consc. – Conscientiousness; ICH – intracerebral hemorrhage.

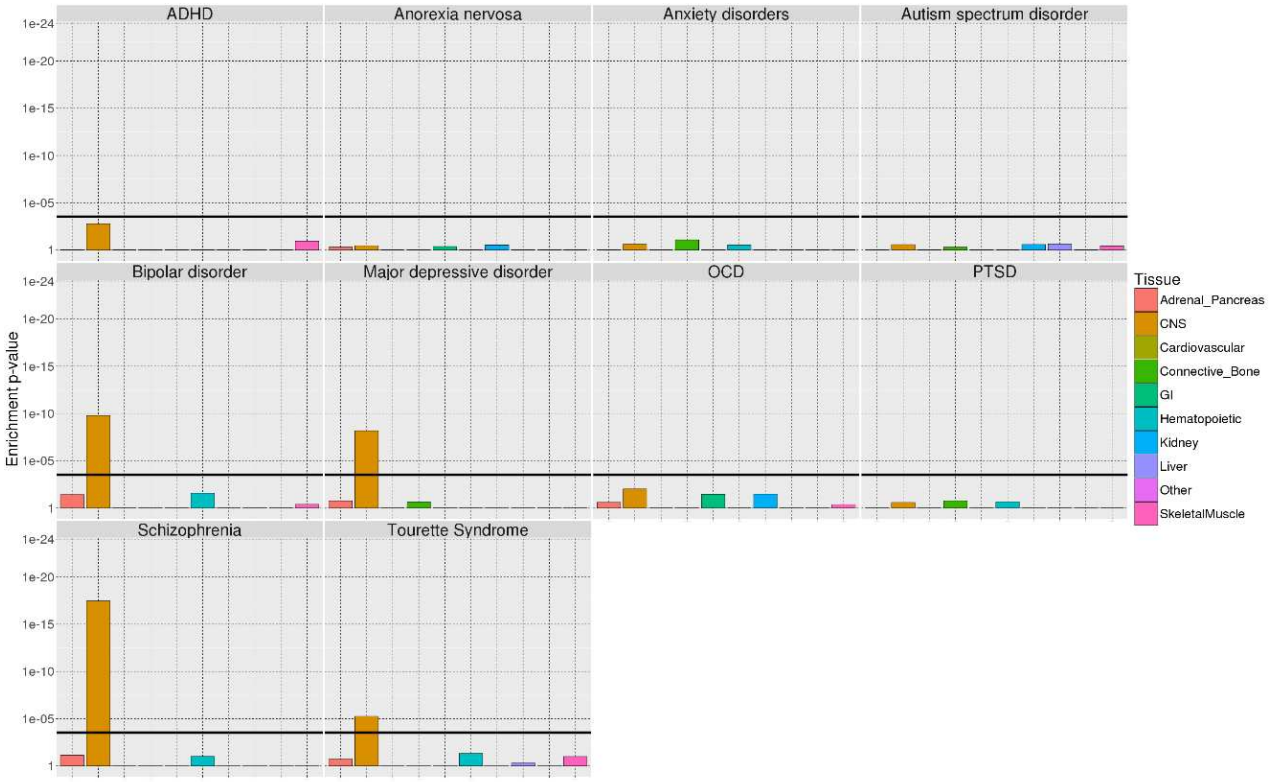


Fig. S7A. Tissue category heritability enrichment analysis in psychiatric phenotypes
ADHD – attention deficit hyperactivity disorder; CNS – central nervous system; GI – gastro-intestinal system; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. Results for largely overlapping dataset in schizophrenia has been previously reported in Finucane et al(*92*). Black line denotes significance threshold for Bonferroni multiple testing correction, $p=2.81 \times 10^{-4}$. Only positive enrichment reported.

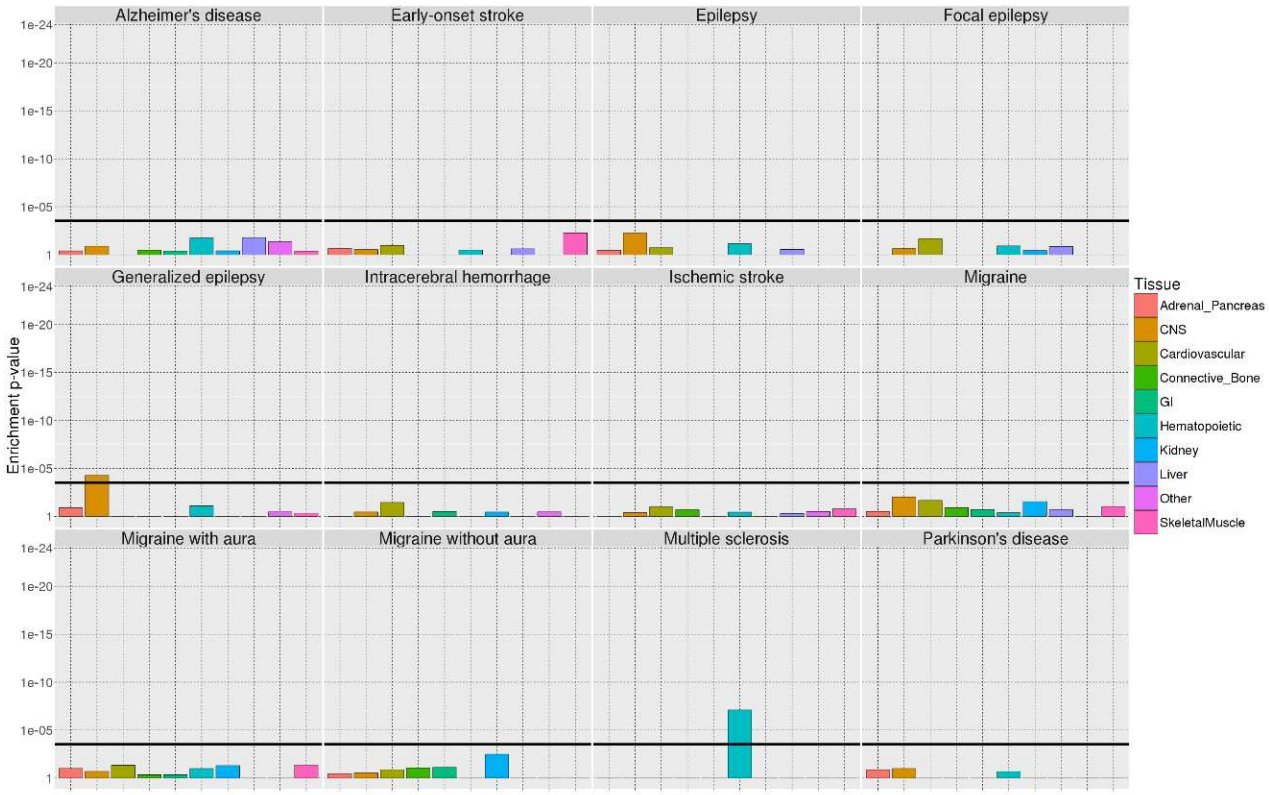


Fig. S7B. Tissue category heritability enrichment analysis in neurological phenotypes

CNS – central nervous system; GI – gastro-intestinal system. Black line denotes significance threshold for Bonferroni multiple testing correction, $p=2.81 \times 10^{-4}$. Only positive enrichment reported.

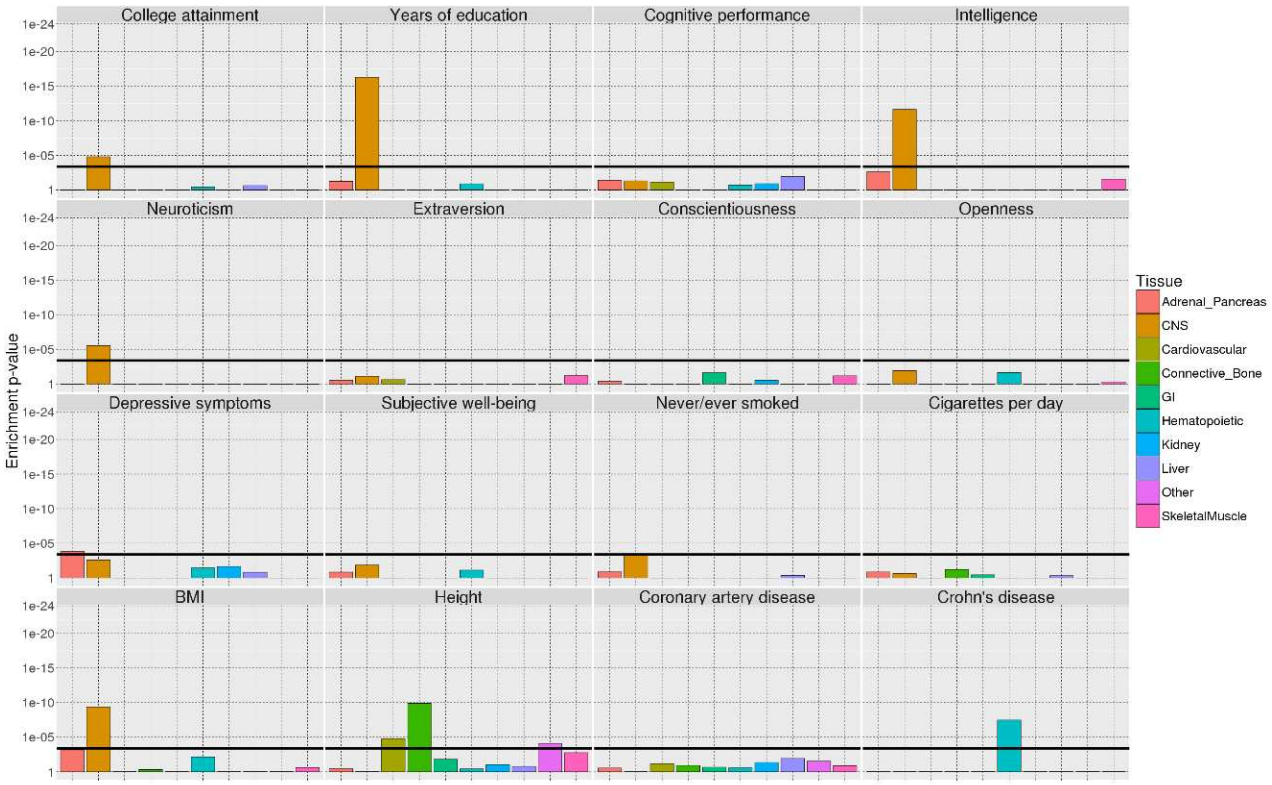


Fig. S7C. Tissue category heritability enrichment analysis in quantitative and additional phenotypes

BMI – body-mass index. CNS – central nervous system; GI – gastro-intestinal system. Results for identical datasets in BMI, Crohn's disease and height have been previously reported in Finucane et al(*92*), and those for depressive symptoms in Okbay et al(*93*). The black line denotes significance threshold for Bonferroni multiple testing correction, $p=4.10 \times 10^{-4}$. Only positive enrichment reported.

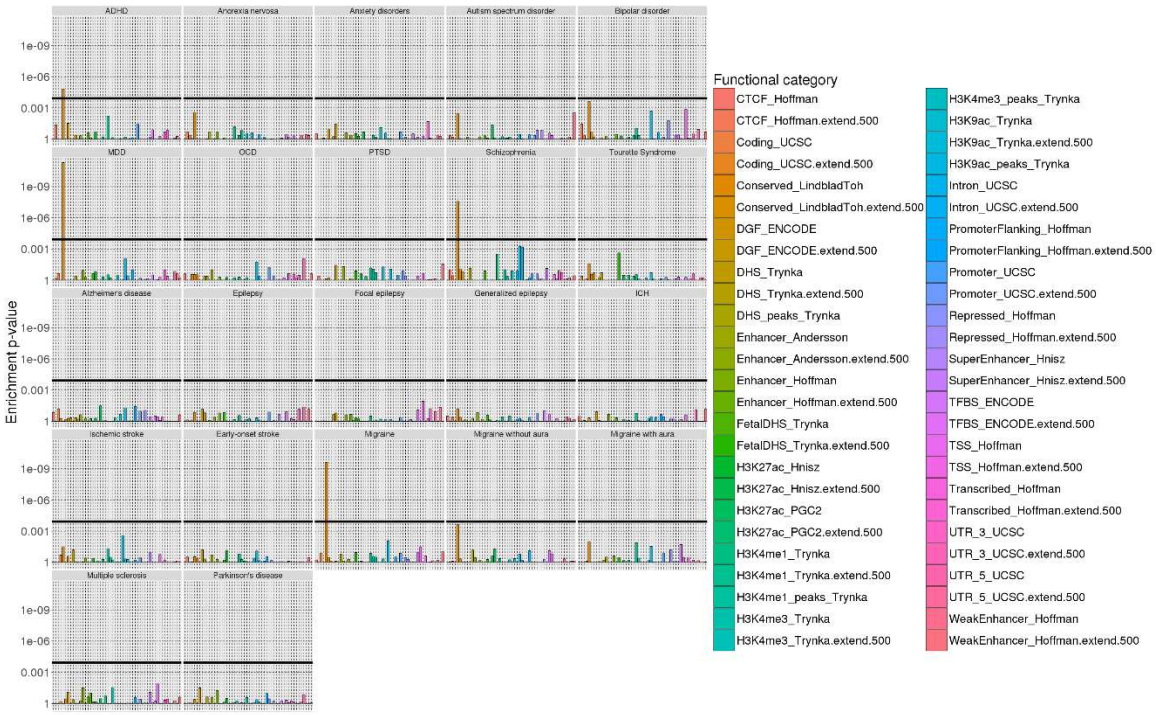


Fig. S7D. Partitioned heritability analysis across 53 functional categories in study disorders

ADHD - attention deficit hyperactivity disorder; ICH – intracerebral hemorrhage; MDD – major depressive disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder. Results for a largely overlapping dataset in schizophrenia have been previously reported in Finucane et al(*92*). The black line denotes significance threshold for Bonferroni multiple testing correction, $p=1.17 \times 10^{-4}$. Only positive enrichment reported.

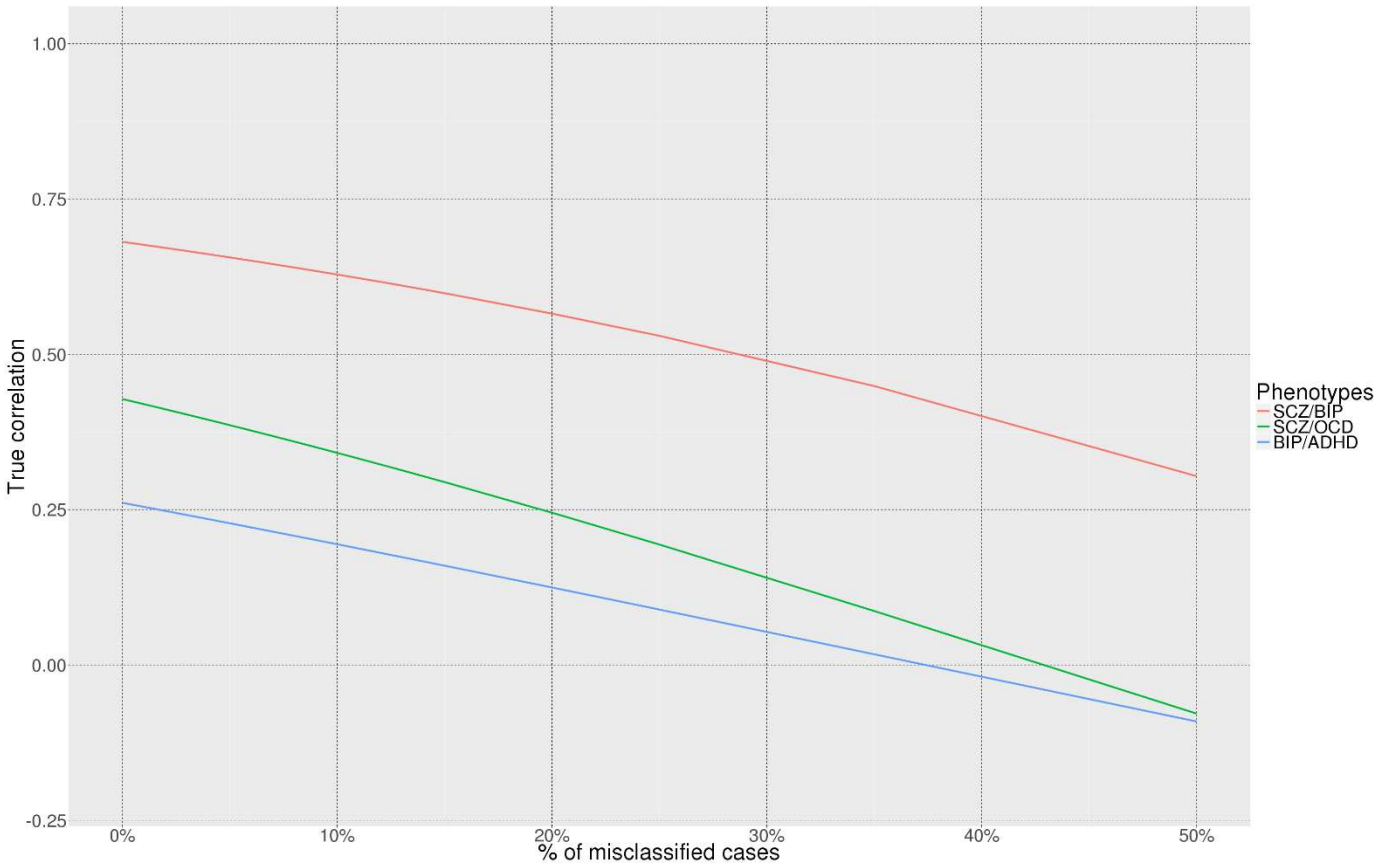


Fig. S8. Effect of case misclassification on true underlying genetic correlation given the observed results.

ADHD - attention deficit hyperactivity disorder; BIP – bipolar disorder; OCD – obsessive-compulsive disorder; SCZ – schizophrenia. Genetic correlations as a function of misclassification based on derivation described in the section "Effect of co-morbidity and phenotypic misclassification on correlation estimates", for the same phenotype pairs as reported in Table S5.

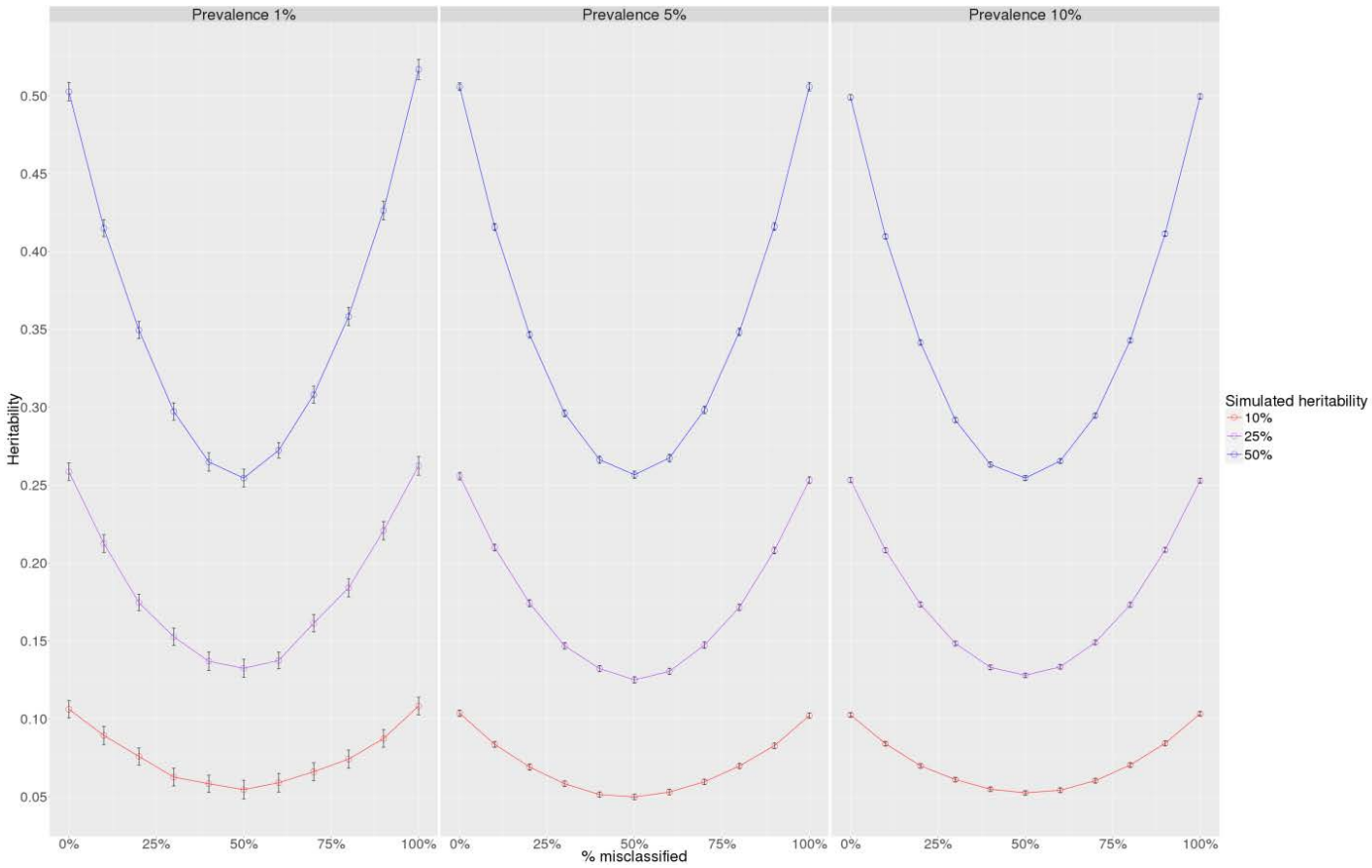


Fig. S9A. Effect of case misclassification on observed heritability

See Supplementary Text "Effect of co-morbidity and phenotypic misclassification on correlation estimates" for details. Error bars show one standard error.

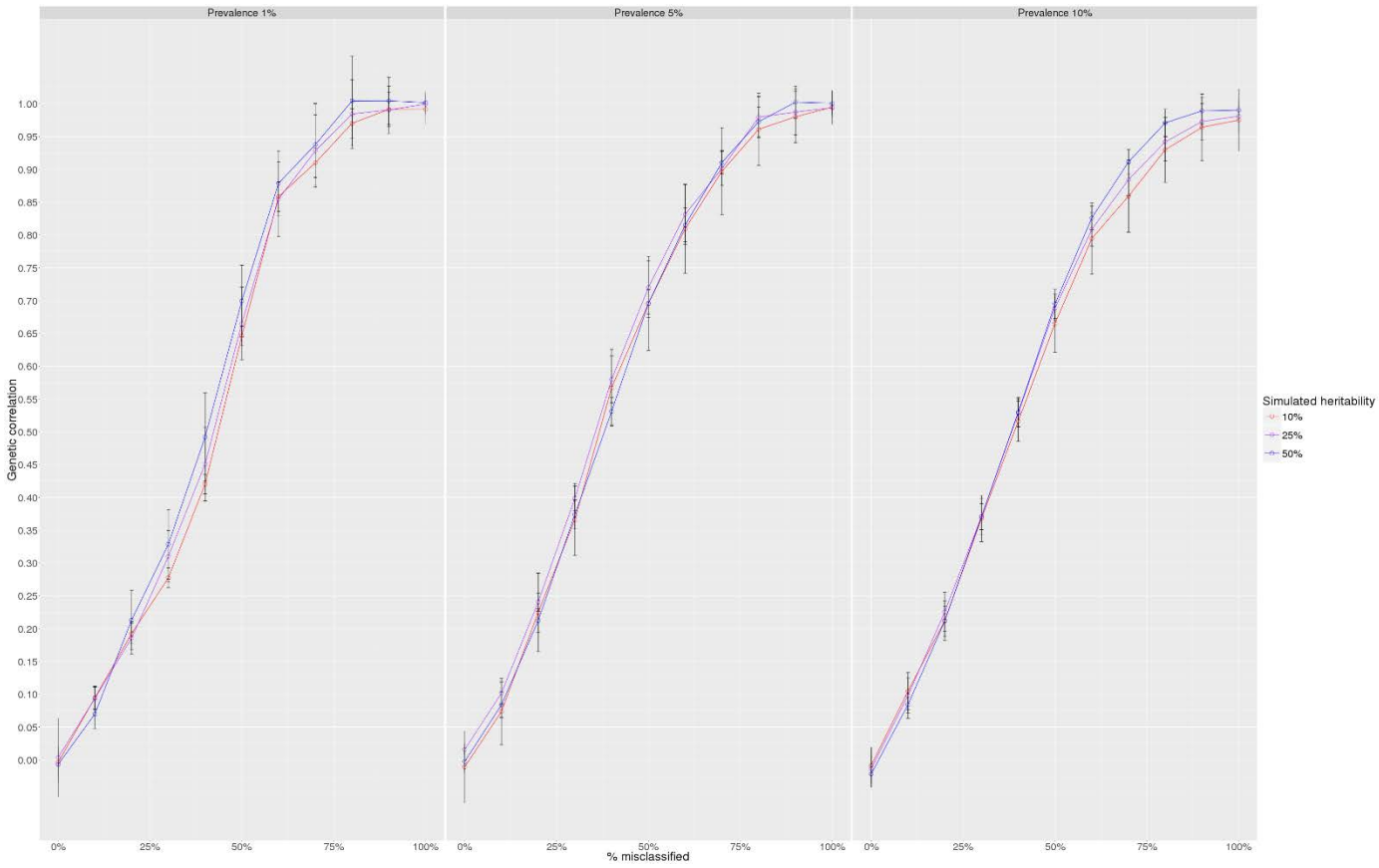


Fig. S9B. Effect of case misclassification on genetic correlation.

See Supplementary Text "Effect of co-morbidity and phenotypic misclassification on correlation estimates" for details. Error bars show one standard error.

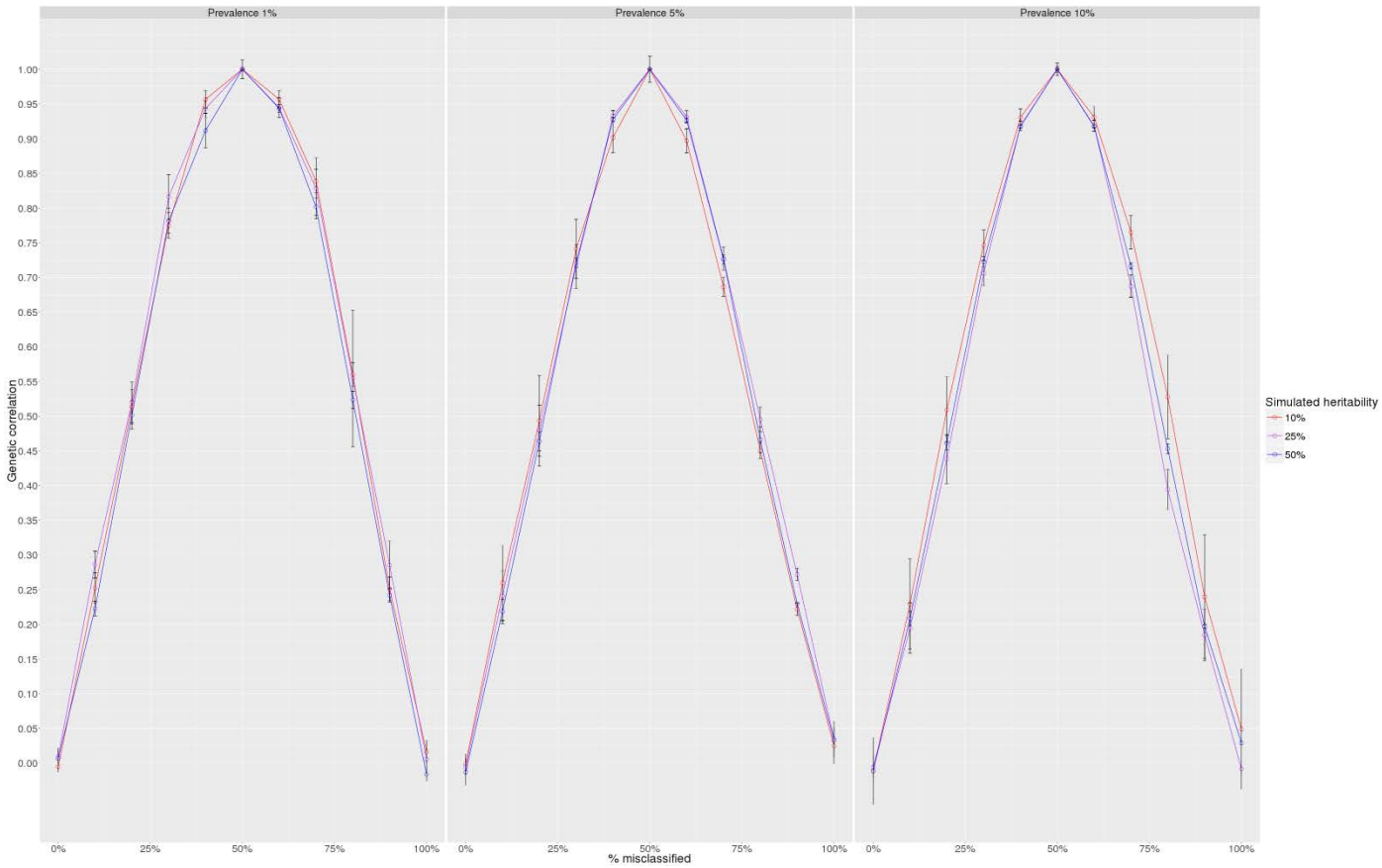


Fig. S9C. Effect of bidirectional case misclassification on genetic correlation

See Supplementary Text "Effect of co-morbidity and phenotypic misclassification on correlation estimates" for details. Error bars show one standard error.

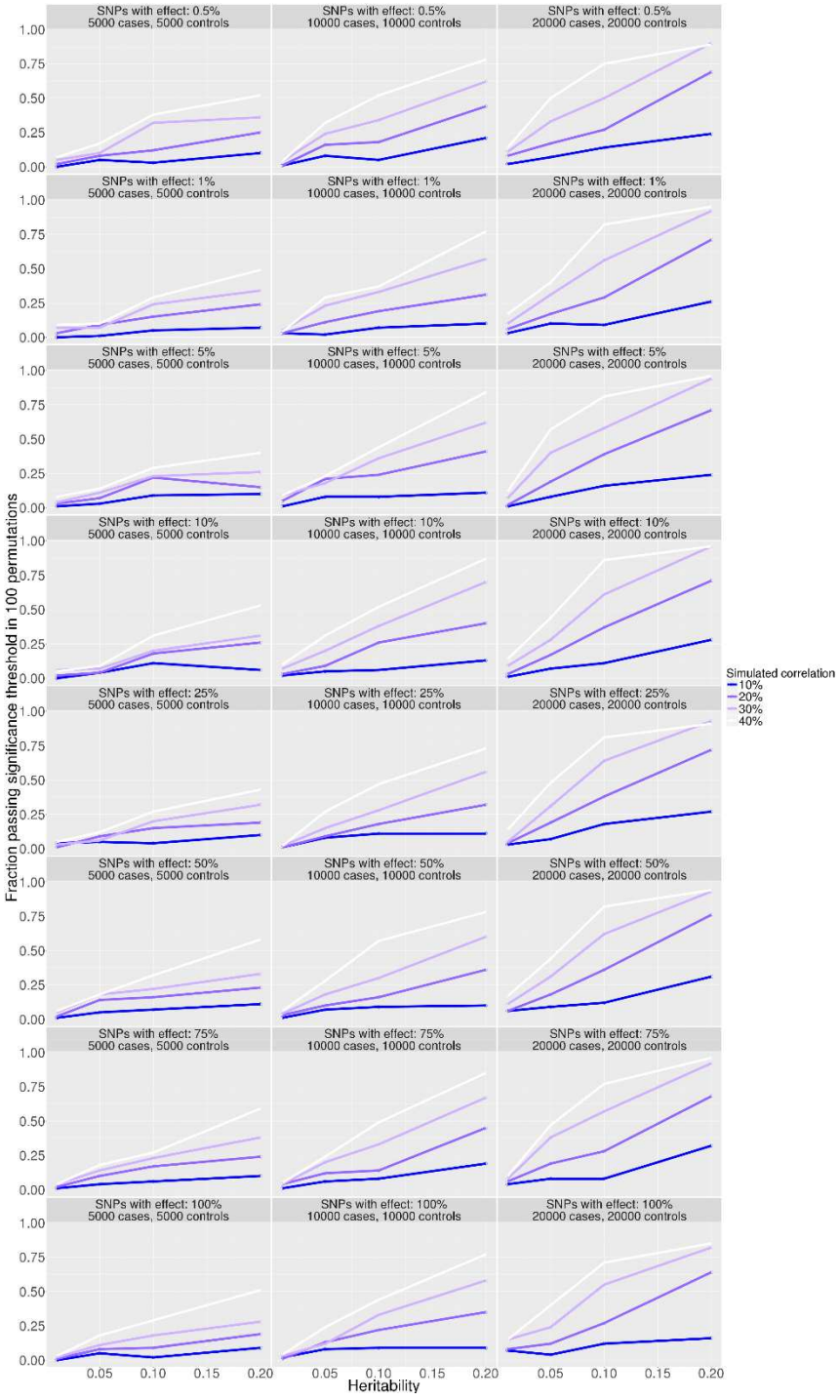


Fig. S10. Power analysis for detecting genetic correlations.

Shown at each combination of parameters is the fraction of simulations out of 100 replicates which detect the simulated correlation between the pair of phenotypes and are within the 95% confidence interval from the true correlation.

Table S1. Dataset features for the brain disorder phenotypes.

ADHD – attention deficit hyperactivity disorder; OCD – obsessive-compulsive disorder; PTSD – post-traumatic stress disorder; Pop. prev. – population prevalence; AOE – average age of onset; GC – genomic control; Publ. – publication for genotype data; MUP – manuscript under preparation; Preval. ref. – publication for prevalence estimate; PC – personal communication. All age of onset estimates based on personal communication and constitute rough estimates. Anxiety disorders refers to a meta-analysis of five subtypes (generalized anxiety disorder, panic disorder, social phobia, agoraphobia and specific phobias; see reference). Numbers in gray denote a dataset which is non-unique, e.g. all cardioembolic stroke cases and controls are also part of ischemic stroke cases and controls, respectively. For genomic control, - : no GC; + : study-level GC; ++ : meta-analysis GC. Note: genomic control will impact the univariate estimate of heritability, but the genetic correlation estimation is robust to genomic control. References are: a(*94*), b(*95*), c(*96*), d(*97*), e(*98*), f(*99*), g(*100*), h(*101*), i(*102*), j(*103*), k(*104*), l(*105*), m(*106*), n(*107*), o(*108*), p(*109*), q(*110*), r(*111*), s(*112*), approximated from t(*113*), approximated from u(*114*), v(*115*), w(*116*), and x(*117*).

Phenotype	Cases	Controls	Pop. prev.	AOE	Heritability (SE)	GC	Mean χ^2	Lambda	Intercept (SE)	Publ.	Preval. ref.
Psychiatric disorders											
ADHD	12,645	84,435	0.050	12	0.100 (0.011)	-	1.102	1.107	1.014 (0.007)	MUP	m
Anorexia nervosa	3,495	11,105	0.006	15	0.172 (0.027)	+	1.077	1.086	1.012 (0.008)	a	n
Anxiety disorders	5,761	11,765	0.100	11	0.112 (0.045)	-	1.035	1.030	1.003 (0.008)	b	o
Autism spectrum disorder	6,197	7,377	0.010	2	0.189 (0.025)	-	1.081	1.071	0.987 (0.009)	c	m
Bipolar disorder	20,352	31,358	0.010	25	0.205 (0.010)	-	1.324	1.387	1.021 (0.010)	MUP	m
Major depressive disorder	16,823	25,632	0.150	32	0.112 (0.006)	-	1.263	1.293	1.005 (0.010)	MUP	m
OCD	2,936	7,279	0.016	16	0.255 (0.037)	-	1.059	1.065	1.000 (0.007)	MUP	p
PTSD	2,424	7,113	0.080	23	0.148 (0.065)	-	1.107	1.102	1.014 (0.007)	d	q
Schizophrenia	33,640	43,456	0.010	21	0.256 (0.010)	-	1.588	1.768	1.059 (0.012)	e	m
Tourette's syndrome	4,220	8,994	0.005	7	0.196 (0.025)	-	1.096	1.103	1.010 (0.007)	MUP	r
Neurological disorders											
Alzheimer's disease	17,008	37,154	0.170	65	0.130 (0.023)	-	1.093	1.104	1.038 (0.007)	f	PC
Epilepsy	7,779	20,439	0.030	25	0.101 (0.022)	+	1.047	1.057	0.993 (0.010)	g	s
Focal epilepsy	4,601	17,985	0.020	15	0.053 (0.026)	+	1.023	1.013	0.988 (0.009)	g	PC
Generalized epilepsy	2,525	16,244	0.008	15	0.351 (0.039)	+	1.065	1.081	0.960 (0.009)	g	PC
Intracerebral hemorrhage	1,545	1,481	0.002	70	0.156 (0.060)	-	1.038	1.037	1.012 (0.007)	h	t
Ischemic stroke	10,307	19,326	0.010	71	0.038 (0.010)	-	1.065	1.066	1.032 (0.006)	i	u
Cardioembolic stroke	1,859	17,708	-	-	-	-	1.061	1.047	1.049 (0.006)	i	-
Early-onset stroke	3,274	11,012	0.003	50	0.051 (0.020)	-	1.029	1.033	1.009 (0.007)	i	PC
Large-vessel disease	1,817	17,708	-	-	-	-	1.061	1.053	1.052 (0.006)	i	-
Small-vessel disease	1,349	17,708	-	-	-	-	1.048	1.047	1.052 (0.006)	i	-
Migraine	59,673	316,078	0.160	30	0.150 (0.007)	-	1.293	1.375	1.036 (0.010)	j	v
Migraine with aura	6,332	142,817	0.075	30	0.124 (0.024)	-	1.077	1.087	1.003 (0.007)	j	w
Migraine without aura	8,348	136,758	0.130	30	0.208 (0.025)	-	1.080	1.085	1.033 (0.007)	j	w
Multiple sclerosis	5,545	12,153	0.002	30	0.141 (0.016)	++	1.050	1.078	0.975 (0.008)	k	x
Parkinson's disease	5,333	12,019	0.002	60	0.105 (0.017)	+	1.026	1.044	0.965 (0.008)	l	x

Table S2. Dataset features for the behavioral-cognitive and additional phenotypes

Numbers in gray denote a sample set which is non-unique, e.g. all samples in the BMI analysis are also part of the height analysis. SE – standard error; Ref. – reference; ISCE - International Standard Classification of Education (1997); NEO-FFI - Neuroticism-Extraversion-Openness Five-Factor Inventory; BMI – body-mass index; CAD – coronary artery disease; MI – myocardial infarction; (d) – dichotomous phenotype; (q) – quantitative phenotype. References are: a(*118*), b(*119*), c(*120*), d(*121*), e(*93*), f(*122*), g(*123*), h(*124*), i(*125*), j(*126*), k(*127*) and l(*128*).

Phenotype	n	Heritability (SE)	Mean χ^2	Lambda	Intercept (SE)	Ref.	Definition
Cognitive measures							
Years of education (q)	293,723	0.302 (0.010)	1.645	1.475	0.938 (0.009)	a	Years of schooling, measured with the ISCE scale
College attainment (d)	120,917	0.109 (0.008)	1.223	1.194	1.021 (0.009)	b	College completion (ISCE scale value >=5)
Cognitive performance (q)	17,989	0.191 (0.031)	1.075	1.065	1.001 (0.009)	c	General cognitive ability in childhood (ages 6-18)
Intelligence (q)	78,308	0.194 (0.010)	1.299	1.260	1.015 (0.008)	d	Intelligence measures (fluid intelligence scores in adults or general cognitive ability in children)
Personality measures							
Subjective well-being (q)	298,420	0.062 (0.005)	1.152	1.130	1.001 (0.007)	e	Self-assessed psychological well-being, based on positive affect or life satisfaction questionnaires
Depressive symptoms (q)	161,460	0.063 (0.005)	1.153	1.133	1.000 (0.007)	e	Score for depressive symptoms, based on positive affect or life satisfaction questionnaires
Neuroticism (q)	170,911	0.125 (0.010)	1.307	1.237	0.994 (0.010)	e	Personality score for neuroticism symptoms, based on positive affect or life satisfaction questionnaires
Extraversion (q)	63,030	0.049 (0.008)	1.073	1.065	1.008 (0.007)	f	Extraversion personality trait, as measured by several different questionnaires
Agreeableness (q)	17,375	-	1.010	0.999	1.001 (0.010)	g	NEO-FFI questionnaire for personality scores
Conscientiousness (q)	17,375	0.070 (0.033)	1.029	1.020	1.001 (0.009)	g	NEO-FFI questionnaire for personality scores
Openness (q)	17,375	0.125 (0.030)	1.037	1.041	0.988 (0.009)	g	NEO-FFI questionnaire for personality scores
Smoking-related measures							
Never/ever smoked (d)	74,035	0.120 (0.010)	1.103	1.090	0.996 (0.006)	h	Lifetime cigarette consumption >= 100
Cigarettes per day (q)	38,617	0.057 (0.013)	1.049	1.053	1.007 (0.006)	h	Average or maximum number of cigarettes per day
Additional phenotypes							
BMI (q)	339,224	0.109 (0.003)	1.158	1.038	0.672 (0.008)	i	BMI, as measured
Height (q)	253,288	0.312 (0.014)	2.949	2.001	1.325 (0.019)	j	Height, as measured
Coronary artery disease (d)	86,995	0.098 (0.013)	1.145	1.105	1.027 (0.009)	k	Presence of CAD, MI, or both
Crohn's disease (d)	20,883	0.177 (0.021)	1.242	1.143	1.028 (0.012)	l	Presence of Crohn's disease

Table S3. Comparison of heritability estimates in this study with previously reported estimates based on SNP data.

ADHD – attention deficit hyperactivity disorder; ESS – effective sample size; OCD – obsessive-compulsive disorder; SE – standard error. References previous reports are: a(*106*), b(*95*), c(*129*), d(*97*), e(*130*), f(*131*), g(*132*), h(*133*), and i(*134*). * - Previously reported heritability for anxiety disorders is an LDSC analysis of the same dataset; difference between the estimates is due to the current study estimating heritability under unscreened controls.

	Previously reported		*Current study*		
Phenotype	Heritability (SE)	ESS	Heritability (SE)	ESS	Reference
Psychiatric disorders					
ADHD	0.28 (0.023)	12,374	0.100 (0.011)	43,992	a
Anorexia nervosa	-	-	0.172 (0.027)	10,633	-
Anxiety disorders*	0.10 (0.037)	15,469	0.112 (0.045)	15,469	b
Autism spectrum disorder	0.17 (0.025)	6,729	0.189 (0.025)	10,610	a
Bipolar disorder	0.25 (0.012)	15,391	0.205 (0.010)	49,367	a
Major depressive disorder	0.21 (0.021)	18,416	0.112 (0.006)	40,627	a
OCD	0.37 (0.070)	3,394	0.255 (0.037)	8,369	c
PTSD*	0.15(0.060)	7,232	0.148 (0.065)	7,232	d
Schizophrenia	0.23 (0.008)	20,811	0.256 (0.010)	75,846	a
Tourette's syndrome	0.58 (0.090)	2,146	0.196 (0.025)	11,489	c
Neurological disorders			0.130 (0.023)		
Alzheimer's disease	0.24 (0.030)	7,095	0.101 (0.022)	46,669	e
Epilepsy	0.32 (0.046)	4,041	0.053 (0.026)	22,538	f
Focal epilepsy	0.23 (0.102)	3,229	0.351 (0.039)	14,655	f
Generalized epilepsy	0.36 (0.117)	1,134	0.156 (0.060)	8,741	f
Intracerebral hemorrhage	0.29 (0.110)	1,663	0.038 (0.010)	3,025	g
Ischemic stroke	0.38 (0.052)	8,025	-	26,888	h
Cardioembolic stroke	0.33 (0.074)	2,592	0.051 (0.020)	6,730	h
Early-onset stroke	-	-	-	10,095	h
Large-vessel disease	0.40 (0.076)	2,698	-	6,592	-
Small-vessel disease	0.16 (0.077)	1,993	0.150 (0.007)	5,014	h
Migraine	-	-	0.124 (0.024)	200,785	-
Migraine with aura	-	-	0.208 (0.025)	24,253	-
Migraine without aura	-	-	0.141 (0.016)	31,471	-
Multiple sclerosis	0.30 (0.030)	3,523	0.105 (0.017)	15,231	e
Parkinson's disease	0.27 (0.053)	20,798	0.105 (0.017)	14,776	i

Table S4. Heritability estimates and selected study variables in weighted-least squares analysis.

P-values are uncorrected for multiple testing. Age of onset refers to the average age of onset of the disorder. Asterisk indicates results which are significant after Bonferroni correction for four tests.

Study feature	F-statistic	Adjusted R^2	P-value
Case/control ratio	0.534	-0.023	0.474
Effective sample size	1.039	0.002	0.320
Phenotype prevalence	0.341	-0.032	0.566
Age of onset	10.280	0.307	0.004*

Table S5. Implied true correlations between selected phenotypes, given co-morbidity estimates from literature.

ADHD – attention deficit hyperactivity disorder; OCD – obsessive-compulsive disorder. References used for λ values (proportion of cases correctly called cases) are a (*135*), b(*136*), c(*137*). From reference a, λ was calculated by summing over all relevant disorder progression paths. See Supplementary text ("Effect of co-morbidity and phenotypic misclassification on correlation estimates") for further details.

Phenotype 1	Phenotype 2	True r_g	Observed r_g	λ	$h_{1,obs}$	h_2	Reference
Schizophrenia	Bipolar disorder	0.654	0.681	0.946	0.506	0.453	a
Schizophrenia	OCD	0.120	0.428	0.683	0.506	0.505	b
Bipolar disorder	ADHD	0.043	0.261	0.686	0.453	0.316	c
Bipolar disorder	Schizophrenia	0.514	0.681	0.808	0.453	0.506	a

Table S6. Proportions of unidirectional misclassification.

Listed are the proportions of unidirectional misclassification which would be required to reach the observed genetic correlation under the assumption of no true genetic correlation for the significantly correlated disorder-disorder pairs in this study, in order of decreasing significance. ADHD – attention deficit hyperactivity disorder; ASD – autism spectrum disorder; MDD – major depressive disorder; OCD – obsessive-compulsive disorder. Type-subtype pairs (e.g. epilepsy and focal epilepsy) have been excluded.

Phenotype 1	Phenotype 2	Observed r_g	Misclassification %
Bipolar disorder	Schizophrenia	0.681	54.5%
MDD	Schizophrenia	0.338	14.8%
Bipolar disorder	MDD	0.351	64.2%
MDD	Migraine	0.323	24.8%
ADHD	MDD	0.521	46.5%
OCD	Schizophrenia	0.327	32.6%
ADHD	Migraine	0.261	17.9%
Anxiety disorders	MDD	0.794	79.4%
ADHD	Schizophrenia	0.223	8.7%
OCD	Tourette Syndrome	0.428	55.7%
Bipolar disorder	OCD	0.311	25.0%
ADHD	Bipolar disorder	0.261	12.7%
Anorexia nervosa	OCD	0.517	34.9%
Migraine	Tourette Syndrome	0.192	14.3%
MDD	Migraine without aura	0.225	12.2%
Anorexia nervosa	Schizophrenia	0.219	14.7%
MDD	Migraine with aura	0.278	29.4%
MDD	Tourette Syndrome	0.213	12.2%
MDD	OCD	0.228	10.0%
ASD	Schizophrenia	0.208	15.5%

Table S7 (separate file). Disorder-disorder (A), disorder-phenotype (B) and phenotype-phenotype (C) correlation results.

Table S8. Tissue enrichment analysis for brain disorders.

Results shown for phenotype-tissue pairs where P-value for enrichment coefficient p-value below the Bonferroni threshold ($p < 2.81 \times 10^{-4}$; data for all pairs in Table S12A). CNS – central nervous system; Coeff. – coefficient; SE – standard error. Results for schizophrenia in a largely overlapping dataset have been previously reported in Finucane et al (38).

Phenotype	Tissue	Enrichment	SE	Coeff.	SE	Coeff. p-value
Schizophrenia	CNS	3.25	0.18	1.65E-07	1.92E-08	3.35E-18
Bipolar disorder	CNS	3.81	0.32	1.43E-07	2.28E-08	1.69E-10
Major depressive disorder	CNS	2.76	0.30	2.03E-08	3.58E-09	6.73E-09
Multiple sclerosis	Hematopoietic	4.90	0.54	2.85E-07	5.44E-08	8.03E-08
Tourette Syndrome	CNS	4.23	0.78	2.32E-07	5.29E-08	5.67E-06
Generalized epilepsy	CNS	2.79	0.60	1.68E-07	4.34E-08	5.44E-05

Table S9. Tissue enrichment analysis for behavioral-cognitive phenotypes and additional traits

Results shown for phenotype-tissue pairs where P-value for enrichment coefficient p-value below the Bonferroni threshold ($p < 4.10 \times 10^{-4}$; data for all pairs in Table S12A). BMI – body-mass index; CNS – central nervous system; Coeff. – coefficient; SE – standard error. Results for the same dataset in height, BMI and Crohn's disease have been previously reported in Finucane et al (38), and depressive symptoms in Okbay et al(*93*).

Phenotype	Tissue	Enrichment	SE	Coeff.	SE	Coeff. p-value
Years of education	CNS	2.87	0.19	9.51E-08	1.15E-08	5.66E-17
Intelligence	CNS	3.38	0.31	8.34E-08	1.20E-08	2.26E-12
Height	Connective_Bone	5.32	0.38	2.24E-07	3.55E-08	1.31E-10
BMI	CNS	2.67	0.18	2.73E-08	4.46E-09	4.39E-10
Crohn's disease	Hematopoietic	4.19	0.43	3.60E-07	6.66E-08	3.15E-08
Neuroticism	CNS	2.47	0.29	3.83E-08	8.45E-09	2.95E-06
College attainment	CNS	3.31	0.45	2.71E-08	6.52E-09	1.59E-05
Height	Cardiovascular	4.23	0.38	1.28E-07	3.08E-08	1.66E-05
Height	Other	3.42	0.21	8.26E-08	2.19E-08	7.84E-05
Depressive symptoms	Adrenal_Pancreas	5.15	0.94	3.77E-08	1.04E-08	1.47E-04
Never/ever smoked	CNS	3.45	0.73	3.06E-08	9.13E-09	4.04E-04

Table S10. Functional category enrichment analysis for brain disorders

Results shown for phenotype-tissue pairs where P-value for enrichment coefficient p-value below the Bonferroni threshold ($p < 1.17 \times 10^{-4}$; data for all pairs in Table S12B). ADHD – attention deficit hyperactivity disorder; Coeff. – coefficient; SE – standard error. Results for schizophrenia in a largely overlapping dataset have been previously reported in Finucane et al (38).

Phenotype	Category	Enrichment	SE	Coeff.	SE	Coeff. p-value
Major depressive disorder	Conserved_LindbladToh	19.14	2.50	1.74E-07	2.52E-08	2.42E-12
Migraine	Conserved_LindbladToh	16.88	2.08	1.09E-07	1.72E-08	1.15E-10
Schizophrenia	Conserved_LindbladToh	11.03	1.55	6.73E-07	1.21E-07	1.27E-08
ADHD	Conserved_LindbladToh	27.15	6.24	2.00E-07	4.61E-08	7.46E-06
Migraine without aura	Conserved_LindbladToh	20.64	4.99	9.63E-08	2.61E-08	1.12E-04
Bipolar disorder	Conserved_LindbladToh	9.95	1.98	3.80E-07	1.03E-07	1.17E-04

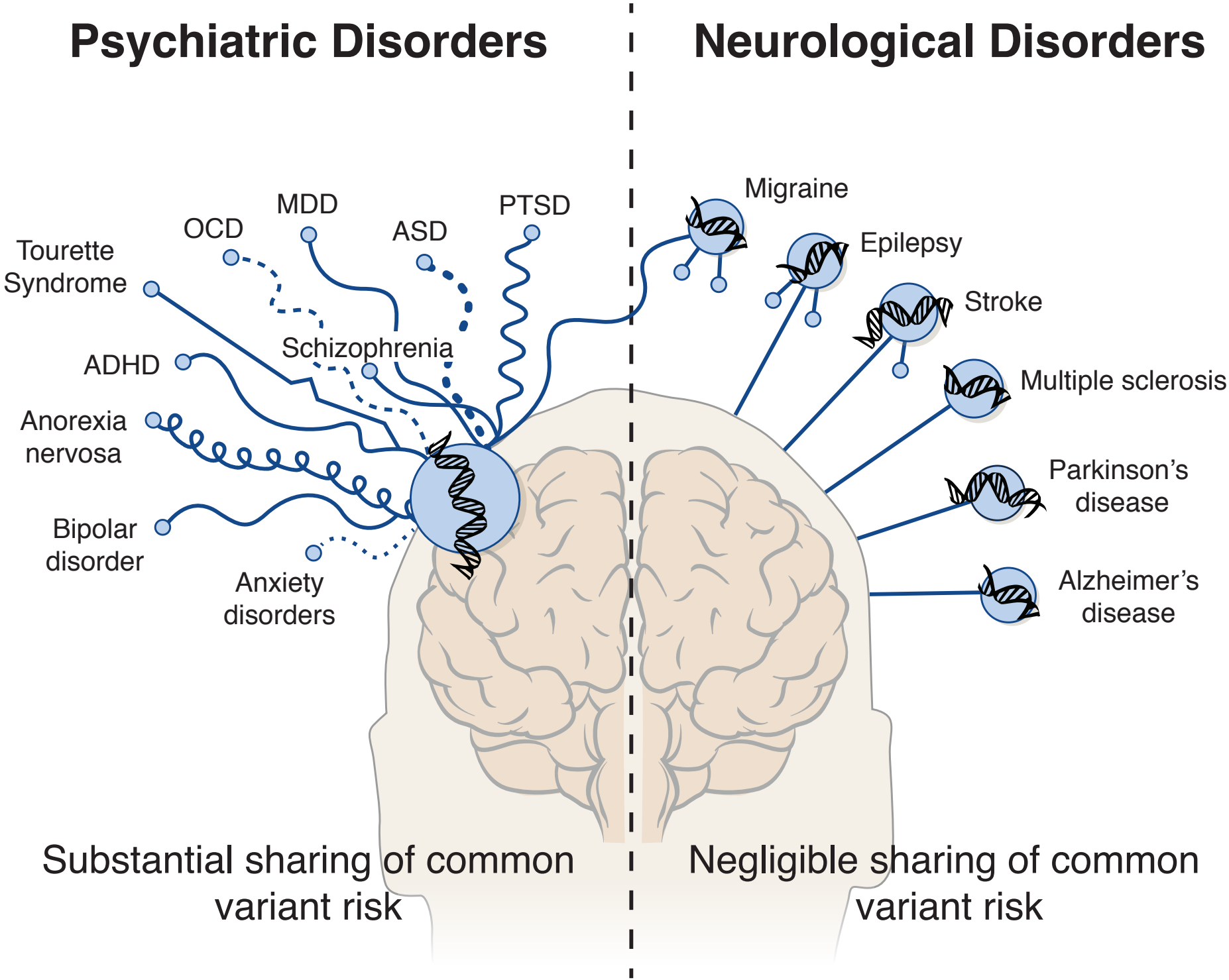
Table S11. Functional category enrichment analysis for behavioral-cognitive phenotypes and additional traits

Results shown for phenotype-tissue pairs where P-value for enrichment coefficient p-value below the Bonferroni threshold ($p < 1.71 \times 10^{-4}$; data for all pairs in Table S12B). BMI – body-mass index; Coeff. – coefficient; SE – standard error. Results for the same dataset in height and BMI have been previously reported in Finucane et al (38).

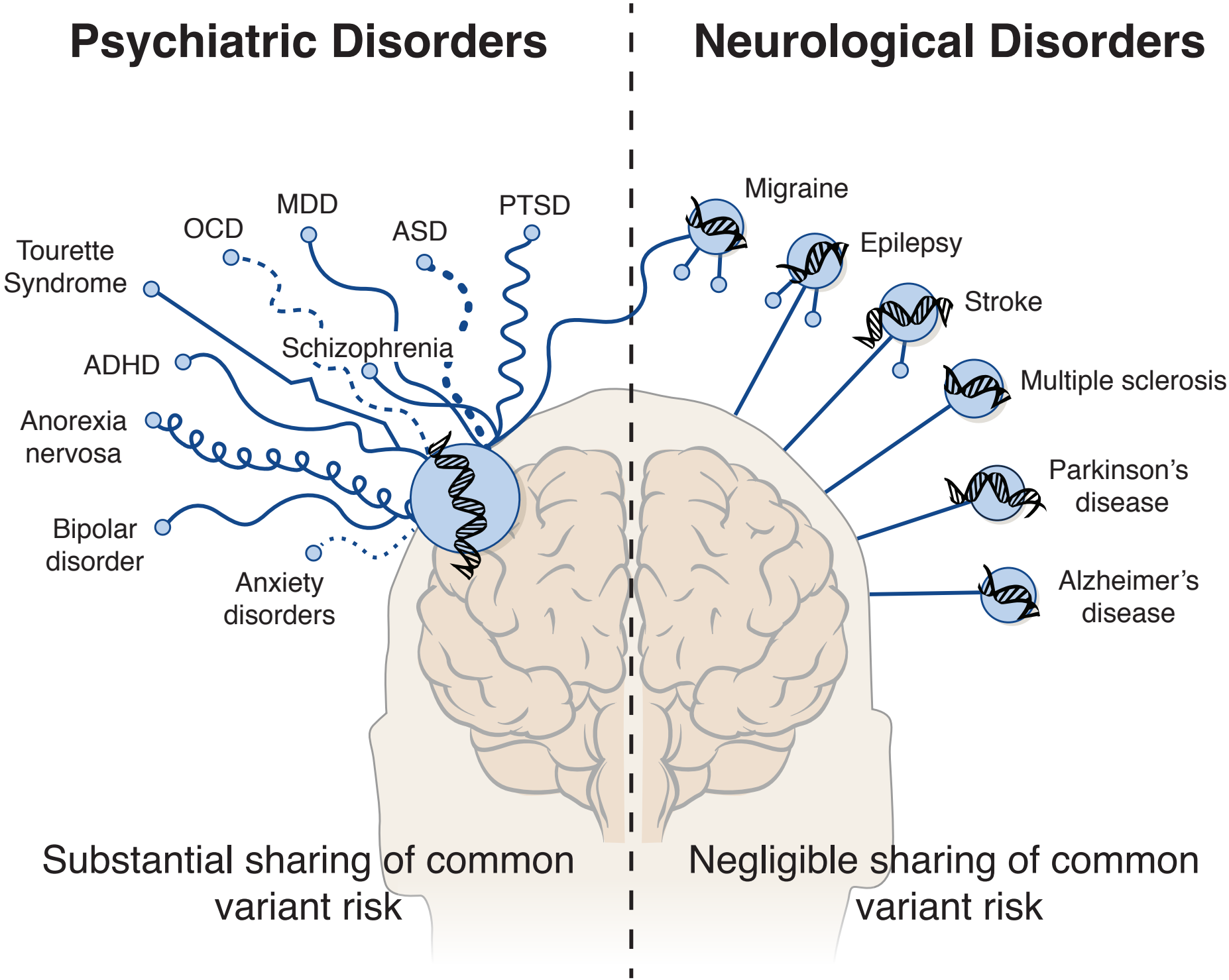
Phenotype	Category	Enrichment	SE	Coeff.	SE	Coeff. p-value
BMI	Conserved_LindbladToh	16.68	1.69	2.76E-07	3.34E-08	7.28E-17
Years of education	Conserved_LindbladToh	14.96	1.68	6.56E-07	8.80E-08	4.67E-14
Height	Conserved_LindbladToh	11.07	1.59	5.15E-07	9.79E-08	7.20E-08
BMI	H3K9ac_peaks_Trynka	7.00	0.97	1.18E-07	2.41E-08	4.79E-07
Neuroticism	Conserved_LindbladToh	11.96	2.95	2.26E-07	5.10E-08	4.50E-06
Intelligence	Conserved_LindbladToh	13.50	2.56	3.51E-07	8.24E-08	9.77E-06
College attainment	Conserved_LindbladToh	16.32	3.31	1.61E-07	3.92E-08	1.98E-05

Table S12 (separate file). Tissue (A) and functional category (B) enrichment analysis results for brain disorders, behavioral-cognitive phenotypes, and additional traits.

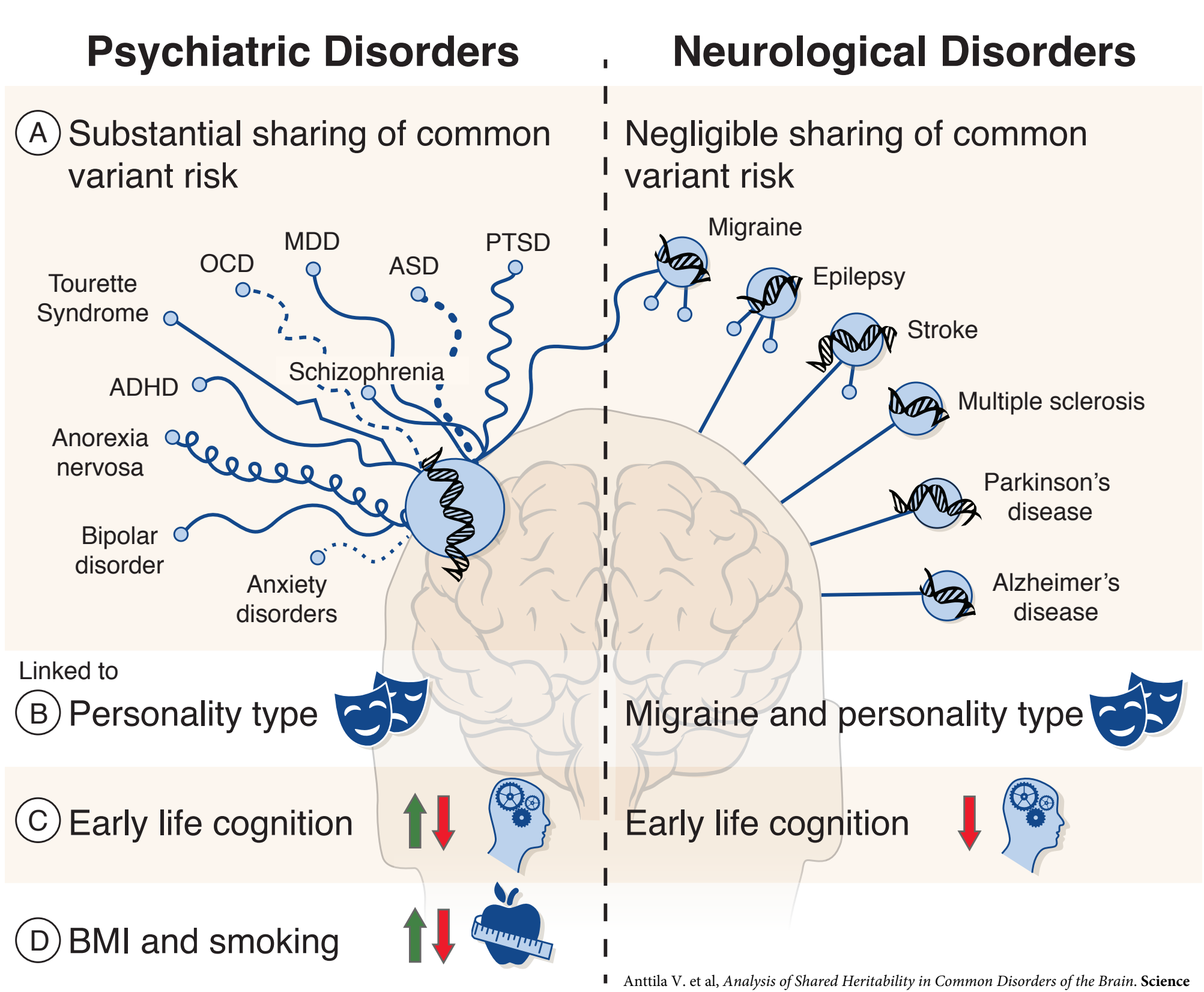
Table S13 (separate file). Data sources, responsible consortia, and data availability.



Anttila V. et al, Analysis of Shared Heritability in Common Disorders of the Brain. **Science.**



Anttila V. et al, Analysis of Shared Heritability in Common Disorders of the Brain. **Science.**



Anttila V. et al, *Analysis of Shared Heritability in Common Disorders of the Brain*. **Science**

Supplementary Table 7A: Disorder-disorder correlations.

Phenotype 1	Phenotype 2	Correlation	Correlation SE	P-value
ADHD	Alzheimer's disease	0.0845	-0.0945	0.3713
ADHD	Anorexia nervosa	-0.2135	-0.1048	0.0417
ADHD	Anxiety disorders	0.398	-0.1882	0.0345
ADHD	Autism spectrum disorder	0.0809	-0.0958	0.3986
ADHD	Bipolar disorder	0.2612	-0.0581	7.00E-06
ADHD	Epilepsy	0.1408	-0.121	0.2444
ADHD	Focal epilepsy	0.2655	-0.1801	0.1405
ADHD	Generalized epilepsy	0.0665	-0.0872	0.4455
ADHD	Intracerebral hemorrhage	0.134	-0.1433	0.3498
ADHD	Ischemic stroke	0.0438	-0.1214	0.7182
ADHD	Early-onset stroke	-0.0477	-0.1495	0.7498
ADHD	Major depressive disorder	0.5207	-0.0563	2.18E-20
ADHD	Migraine	0.2608	-0.0487	8.81E-08
ADHD	Migraine without aura	0.1703	-0.0759	0.0249
ADHD	Migraine with aura	0.1666	-0.1115	0.1352
ADHD	Multiple sclerosis	-0.0588	-0.0721	0.4148
ADHD	OCD	-0.0668	-0.0945	0.48
ADHD	Parkinson's disease	0.0262	-0.0906	0.7721
ADHD	PTSD	0.4488	-0.1706	8.50E-03
ADHD	Schizophrenia	0.2226	-0.0459	1.22E-06
ADHD	Tourette Syndrome	0.2504	-0.0843	0.003
Alzheimer's disease	Anorexia nervosa	-0.0151	-0.1113	0.8919
Alzheimer's disease	Anxiety disorders	0.077	-0.1783	0.6658
Alzheimer's disease	Autism spectrum disorder	0.0494	-0.0986	0.6162
Alzheimer's disease	Bipolar disorder	-0.0224	-0.0547	0.6821
Alzheimer's disease	Epilepsy	0.1577	-0.1325	0.2339
Alzheimer's disease	Focal epilepsy	0.4709	-0.2483	0.0579
Alzheimer's disease	Generalized epilepsy	-0.0154	-0.0911	0.8659
Alzheimer's disease	Intracerebral hemorrhage	-0.1145	-0.1968	0.5606
Alzheimer's disease	Ischemic stroke	0.1638	-0.1379	0.2348
Alzheimer's disease	Early-onset stroke	-0.0092	-0.1794	0.9592
Alzheimer's disease	Major depressive disorder	0.0414	-0.0696	0.5521
Alzheimer's disease	Migraine	-0.0144	-0.0606	0.8128
Alzheimer's disease	Migraine without aura	0.1054	-0.1042	0.3116
Alzheimer's disease	Migraine with aura	-0.1143	-0.1141	0.3165
Alzheimer's disease	Multiple sclerosis	-0.0394	-0.0832	0.6355
Alzheimer's disease	OCD	-0.0898	-0.1102	0.4152
Alzheimer's disease	Parkinson's disease	-0.0747	-0.0957	0.435
Alzheimer's disease	PTSD	-0.091	-0.1918	0.6352
Alzheimer's disease	Schizophrenia	0.0328	-0.0457	0.4722
Alzheimer's disease	Tourette Syndrome	0.0593	-0.0808	0.463
Anorexia nervosa	Anxiety disorders	0.0711	-0.203	0.7262
Anorexia nervosa	Autism spectrum disorder	0.0338	-0.1007	0.7371
Anorexia nervosa	Bipolar disorder	0.1904	-0.057	0.0008
Anorexia nervosa	Epilepsy	0.0405	-0.1357	0.7653
Anorexia nervosa	Focal epilepsy	-0.0019	-0.2159	0.993
Anorexia nervosa	Generalized epilepsy	0.0951	-0.1039	0.3602

Anorexia nervosa	Intracerebral hemorrhage	-0.399	-0.2034	0.0498
Anorexia nervosa	Ischemic stroke	-0.1623	-0.17	0.3396
Anorexia nervosa	Early-onset stroke	-0.3669	-0.2139	0.0862
Anorexia nervosa	Major depressive disorder	0.1599	-0.0663	0.0159
Anorexia nervosa	Migraine	0.0115	-0.0629	0.8555
Anorexia nervosa	Migraine without aura	0.0349	-0.0927	0.7068
Anorexia nervosa	Migraine with aura	0.2318	-0.1097	3.46E-02
Anorexia nervosa	Multiple sclerosis	-0.0098	-0.0818	0.9043
Anorexia nervosa	OCD	0.5168	-0.1172	1.04E-05
Anorexia nervosa	Parkinson's disease	0.0006	-0.1073	0.9952
Anorexia nervosa	PTSD	-0.0154	-0.1934	0.9365
Anorexia nervosa	Schizophrenia	0.2194	-0.0543	5.35E-05
Anorexia nervosa	Tourette Syndrome	-0.0468	-0.0955	0.6241
Anxiety disorders	Autism spectrum disorder	0.2539	-0.1945	0.1918
Anxiety disorders	Bipolar disorder	0.2091	-0.1139	0.0664
Anxiety disorders	Epilepsy	0.2606	-0.256	0.3086
Anxiety disorders	Focal epilepsy	0.1437	-0.4363	0.7419
Anxiety disorders	Generalized epilepsy	0.1473	-0.1602	0.3579
Anxiety disorders	Intracerebral hemorrhage	0.713	-0.3622	4.90E-02
Anxiety disorders	Ischemic stroke	0.1191	-0.2299	0.6044
Anxiety disorders	Early-onset stroke	0.1377	-0.2734	0.6146
Anxiety disorders	Major depressive disorder	0.7939	-0.159	5.97E-07
Anxiety disorders	Migraine	0.2417	-0.1042	0.0203
Anxiety disorders	Migraine without aura	0.2811	-0.1751	0.1084
Anxiety disorders	Migraine with aura	0.3014	-0.2155	0.1618
Anxiety disorders	Multiple sclerosis	0.0699	-0.1618	0.6659
Anxiety disorders	OCD	0.3745	-0.2084	0.0724
Anxiety disorders	Parkinson's disease	-0.0642	-0.1631	0.6939
Anxiety disorders	PTSD	-0.0028	-0.3413	0.9934
Anxiety disorders	Schizophrenia	0.2582	-0.0898	0.004
Anxiety disorders	Tourette Syndrome	0.1925	-0.1572	0.2207
Autism spectrum disorder	Bipolar disorder	0.0968	-0.0665	0.1455
Autism spectrum disorder	Epilepsy	-0.3372	-0.13	0.0095
Autism spectrum disorder	Focal epilepsy	-0.5292	-0.2346	0.0241
Autism spectrum disorder	Generalized epilepsy	-0.167	-0.095	0.0788
Autism spectrum disorder	Intracerebral hemorrhage	0.1239	-0.1904	0.5151
Autism spectrum disorder	Ischemic stroke	-0.1517	-0.1254	0.2265
Autism spectrum disorder	Early-onset stroke	-0.2436	-0.1631	0.1354
Autism spectrum disorder	Major depressive disorder	0.1552	-0.0602	0.0099
Autism spectrum disorder	Migraine	-0.077	-0.0516	0.1355
Autism spectrum disorder	Migraine without aura	0.1578	-0.0898	0.0788
Autism spectrum disorder	Migraine with aura	-0.0647	-0.108	0.549
Autism spectrum disorder	Multiple sclerosis	0.0243	-0.0839	0.7721
Autism spectrum disorder	OCD	0.001	-0.1064	0.9924
Autism spectrum disorder	Parkinson's disease	-0.1961	-0.1012	0.0525
Autism spectrum disorder	PTSD	0.0346	-0.1926	0.8575
Autism spectrum disorder	Schizophrenia	0.2082	-0.0577	0.0003
Autism spectrum disorder	Tourette Syndrome	0.0582	-0.0877	0.5067
Bipolar disorder	Epilepsy	-0.0839	-0.0719	0.2433
Bipolar disorder	Focal epilepsy	-0.0761	-0.1056	4.71E-01

Bipolar disorder	Generalized epilepsy	-0.0595	-0.0562	0.2896
Bipolar disorder	Intracerebral hemorrhage	-0.023	-0.1114	0.8363
Bipolar disorder	Ischemic stroke	0.178	-0.091	0.0506
Bipolar disorder	Early-onset stroke	0.2083	-0.1025	0.0423
Bipolar disorder	Major depressive disorder	0.3507	-0.0318	2.75E-28
Bipolar disorder	Migraine	-0.0251	-0.0302	0.4065
Bipolar disorder	Migraine without aura	-0.0486	-0.0532	3.61E-01
Bipolar disorder	Migraine with aura	0.001	-0.0676	0.9886
Bipolar disorder	Multiple sclerosis	0.0001	-0.0503	9.98E-01
Bipolar disorder	OCD	0.3108	-0.068	4.93E-06
Bipolar disorder	Parkinson's disease	0.0773	-0.0567	0.1724
Bipolar disorder	PTSD	0.0672	-0.0911	0.4608
Bipolar disorder	Schizophrenia	0.6808	-0.021	2.1E-230
Bipolar disorder	Tourette Syndrome	0.0309	-0.053	0.5597
Epilepsy	Focal epilepsy	0.6176	-0.1233	5.51E-07
Epilepsy	Generalized epilepsy	0.7719	-0.0587	1.53E-39
Epilepsy	Intracerebral hemorrhage	0.1541	-0.223	0.4896
Epilepsy	Ischemic stroke	0.3885	-0.2484	0.1178
Epilepsy	Early-onset stroke	0.3694	-0.225	0.1006
Epilepsy	Major depressive disorder	0.1706	-0.0816	0.0366
Epilepsy	Migraine	0.219	-0.0722	0.0024
Epilepsy	Migraine without aura	0.0912	-0.1296	0.4818
Epilepsy	Migraine with aura	0.4665	-0.1491	0.0018
Epilepsy	Multiple sclerosis	-0.048	-0.1297	0.7114
Epilepsy	OCD	-0.4081	-0.1283	0.0015
Epilepsy	Parkinson's disease	0.0459	-0.141	0.7448
Epilepsy	PTSD	0.1534	-0.2453	0.5318
Epilepsy	Schizophrenia	-0.0268	-0.0649	0.6798
Epilepsy	Tourette Syndrome	-0.1876	-0.1159	0.1054
Focal epilepsy	Generalized epilepsy	0.1549	-0.1796	0.3884
Focal epilepsy	Intracerebral hemorrhage	0.806	-0.3949	0.0412
Focal epilepsy	Ischemic stroke	0.6156	-0.3947	0.1189
Focal epilepsy	Early-onset stroke	0.7506	-0.401	0.0612
Focal epilepsy	Major depressive disorder	0.3305	-0.1413	0.0194
Focal epilepsy	Migraine	0.3351	-0.1294	0.0096
Focal epilepsy	Migraine without aura	0.3295	-0.2065	0.1106
Focal epilepsy	Migraine with aura	0.6517	-0.2624	0.013
Focal epilepsy	Multiple sclerosis	0.0504	-0.1993	0.8004
Focal epilepsy	OCD	-0.4762	-0.2284	0.0371
Focal epilepsy	Parkinson's disease	0.1685	-0.2197	0.443
Focal epilepsy	PTSD	0.3863	-0.3735	0.3009
Focal epilepsy	Schizophrenia	-0.0102	-0.0913	0.9114
Focal epilepsy	Tourette Syndrome	-0.3396	-0.1859	0.0678
Generalized epilepsy	Intracerebral hemorrhage	-0.1502	-0.165	0.3627
Generalized epilepsy	Ischemic stroke	-0.0715	-0.1733	0.68
Generalized epilepsy	Early-onset stroke	0.0333	-0.2171	0.878
Generalized epilepsy	Major depressive disorder	0.0231	-0.0645	0.7207
Generalized epilepsy	Migraine	0.0624	-0.0518	0.2284
Generalized epilepsy	Migraine without aura	-0.0494	-0.0981	0.6144
Generalized epilepsy	Migraine with aura	0.1661	-0.1115	0.1362

Generalized epilepsy	Multiple sclerosis	-0.0977	-0.0866	0.2593
Generalized epilepsy	OCD	-0.1928	-0.0931	0.0384
Generalized epilepsy	Parkinson's disease	0.0011	-0.0978	0.9909
Generalized epilepsy	PTSD	0.0827	-0.1507	0.5829
Generalized epilepsy	Schizophrenia	-0.0249	-0.0521	0.6328
Generalized epilepsy	Tourette Syndrome	0.0013	-0.0783	0.9872
Intracerebral hemorrhage	Ischemic stroke	0.4997	-0.2212	0.0239
Intracerebral hemorrhage	Early-onset stroke	0.3607	-0.319	0.2583
Intracerebral hemorrhage	Major depressive disorder	0.1333	-0.1209	2.70E-01
Intracerebral hemorrhage	Migraine	-0.003	-0.0979	0.9754
Intracerebral hemorrhage	Migraine without aura	-0.1632	-0.1773	0.3574
Intracerebral hemorrhage	Migraine with aura	-0.0445	-0.2078	0.8306
Intracerebral hemorrhage	Multiple sclerosis	-0.2004	-0.1483	0.1766
Intracerebral hemorrhage	OCD	0.0987	-0.1686	0.5582
Intracerebral hemorrhage	Parkinson's disease	-0.0577	-0.1725	0.7378
Intracerebral hemorrhage	PTSD	-0.1799	-0.3111	0.563
Intracerebral hemorrhage	Schizophrenia	0.0941	-0.0799	0.2386
Intracerebral hemorrhage	Tourette Syndrome	0.1324	-0.1516	0.3827
Ischemic stroke	Early-onset stroke	1.818	0.308	3.43E-09
Ischemic stroke	Major depressive disorder	0.2263	-0.0953	0.0176
Ischemic stroke	Migraine	0.0835	-0.0809	0.3024
Ischemic stroke	Migraine without aura	-0.0481	-0.1402	0.7317
Ischemic stroke	Migraine with aura	0.2892	-0.1751	0.0986
Ischemic stroke	Multiple sclerosis	0.0823	-0.1119	0.4622
Ischemic stroke	OCD	-0.0142	-0.1322	0.9145
Ischemic stroke	Parkinson's disease	0.1146	-0.1186	0.3338
Ischemic stroke	PTSD	0.6276	-0.2891	0.0299
Ischemic stroke	Schizophrenia	0.2192	-0.0814	7.00E-03
Ischemic stroke	Tourette Syndrome	0.0368	-0.1212	7.61E-01
Early-onset stroke	Major depressive disorder	0.3313	-0.1106	0.0027
Early-onset stroke	Migraine	0.0253	-0.0983	0.7968
Early-onset stroke	Migraine without aura	-0.3	-0.1922	0.1187
Early-onset stroke	Migraine with aura	0.1678	-0.1942	0.3875
Early-onset stroke	Multiple sclerosis	-0.1442	-0.1537	3.48E-01
Early-onset stroke	OCD	-0.0986	-0.1802	0.5842
Early-onset stroke	Parkinson's disease	0.0456	-0.1805	8.00E-01
Early-onset stroke	PTSD	0.2004	-0.3024	5.08E-01
Early-onset stroke	Schizophrenia	0.1106	-0.0771	0.1514
Early-onset stroke	Tourette Syndrome	-0.0448	-0.1532	0.7697
Major depressive disorder	Migraine	0.3232	-0.0331	1.42E-22
Major depressive disorder	Migraine without aura	0.2251	-0.0556	5.23E-05
Major depressive disorder	Migraine with aura	0.278	-0.0715	1.00E-04
Major depressive disorder	Multiple sclerosis	0.0241	-0.0504	6.32E-01
Major depressive disorder	OCD	0.2276	-0.0601	0.0002
Major depressive disorder	Parkinson's disease	0.0794	-0.0586	0.1752
Major depressive disorder	PTSD	0.5192	-0.1492	0.0005
Major depressive disorder	Schizophrenia	0.3377	-0.0282	5.45E-33
Major depressive disorder	Tourette Syndrome	0.2133	-0.055	0.0001
Migraine	Migraine without aura	0.9103	-0.0425	1.1E-101
Migraine	Migraine with aura	1.1103	-0.0917	9.74E-34

Migraine	Multiple sclerosis	0.022	-0.043	0.6091
Migraine	OCD	0.0857	-0.0618	0.1653
Migraine	Parkinson's disease	-0.0258	-0.0542	0.6337
Migraine	PTSD	0.1645	-0.1026	0.1088
Migraine	Schizophrenia	-0.0839	-0.0269	0.0018
Migraine	Tourette Syndrome	0.1916	-0.0447	1.8E-05
Migraine without aura	Migraine with aura	0.4763	-0.111	1.79E-05
Migraine without aura	Multiple sclerosis	0.1787	-0.0852	0.0358
Migraine without aura	OCD	0.0105	-0.0912	9.08E-01
Migraine without aura	Parkinson's disease	-0.0648	-0.0816	4.27E-01
Migraine without aura	PTSD	-0.0699	-0.1628	0.6675
Migraine without aura	Schizophrenia	-0.068	-0.0442	0.1236
Migraine without aura	Tourette Syndrome	0.0503	-0.0819	0.5396
Migraine with aura	Multiple sclerosis	0.0151	-0.0924	0.8699
Migraine with aura	OCD	0.1102	-0.1075	0.3055
Migraine with aura	Parkinson's disease	-0.086	-0.1304	0.5096
Migraine with aura	PTSD	0.1205	-0.2096	0.5654
Migraine with aura	Schizophrenia	-0.0958	-0.0576	0.0963
Migraine with aura	Tourette Syndrome	0.2914	-0.1197	0.0149
Multiple sclerosis	OCD	0.0807	-0.091	0.375
Multiple sclerosis	Parkinson's disease	0.0453	-0.0774	0.5583
Multiple sclerosis	PTSD	0.0385	-0.1427	0.7874
Multiple sclerosis	Schizophrenia	0.0867	-0.0401	0.0308
Multiple sclerosis	Tourette Syndrome	-0.0171	-0.0745	0.8184
OCD	Parkinson's disease	0.1301	-0.1074	0.2256
OCD	PTSD	0.2815	-0.1847	0.1275
OCD	Schizophrenia	0.3273	-0.0588	2.58E-08
OCD	Tourette Syndrome	0.4285	-0.092	3.18E-06
Parkinson's disease	PTSD	0.0253	-0.1949	0.8967
Parkinson's disease	Schizophrenia	0.0545	-0.0534	0.3073
Parkinson's disease	Tourette Syndrome	0.0904	-0.0965	0.3487
PTSD	Schizophrenia	0.1471	-0.088	0.0945
PTSD	Tourette Syndrome	-0.1382	-0.1599	0.3877
Schizophrenia	Tourette Syndrome	0.0627	-0.0416	0.1313

Significance threshold
$p < 3.35 \times 10\text{-}4$

Supplementary Table 12A: Tissue enrichment analysis results for brain disorc

Significant enrichments in bold

Psychiatric disorders

Phenotype	Tissue	Enrichment	SE	Coeff.	SE	Coeff. z-score
Schizophrenia	CNS	3.25	0.18	1.65E-07	1.92E-08	**8.62**
Bipolar disorder	CNS	3.81	0.32	1.43E-07	2.28E-08	**6.28**
Major depressive disorder	CNS	2.76	0.30	2.03E-08	3.58E-09	**5.68**
Tourette Syndrome	CNS	4.23	0.78	2.32E-07	5.29E-08	**4.39**
ADHD	CNS	2.03	0.74	2.02E-08	6.90E-09	2.93
OCD	CNS	3.93	1.08	1.51E-07	6.46E-08	2.34
Autism spectrum disorder	Liver	3.03	1.12	1.96E-07	8.48E-08	2.31
Bipolar disorder	Hematopoietic	1.99	0.22	4.52E-08	2.34E-08	1.93
Autism spectrum disorder	Other	2.20	0.56	1.33E-07	7.21E-08	1.84
OCD	Kidney	8.66	2.78	2.21E-07	1.20E-07	1.84
OCD	GI	3.07	1.10	1.35E-07	7.40E-08	1.82
Bipolar disorder	Adrenal_Pancreas	3.57	0.50	5.69E-08	3.20E-08	1.78
Tourette Syndrome	Hematopoietic	2.18	0.57	9.73E-08	5.81E-08	1.68
Schizophrenia	Adrenal_Pancreas	2.66	0.30	3.95E-08	2.74E-08	1.44
Anxiety disorders	Connective_Bone	12.32	6.99	7.43E-08	5.38E-08	1.38
Schizophrenia	Hematopoietic	1.53	0.16	2.81E-08	2.15E-08	1.31
Tourette Syndrome	SkeletalMuscle	3.06	1.09	1.00E-07	7.87E-08	1.28
ADHD	SkeletalMuscle	1.39	1.05	1.27E-08	1.04E-08	1.22
Autism spectrum disorder	Kidney	2.59	1.69	1.33E-07	1.37E-07	0.97
Major depressive disorder	Adrenal_Pancreas	2.69	0.50	5.91E-09	6.26E-09	0.94
Tourette Syndrome	Adrenal_Pancreas	2.83	1.25	7.17E-08	8.37E-08	0.86
Major depressive disorder	Connective_Bone	1.96	0.41	3.93E-09	5.27E-09	0.74
Anxiety disorders	CNS	8.03	4.33	2.78E-08	3.87E-08	0.72
Autism spectrum disorder	CNS	1.89	0.62	4.13E-08	6.08E-08	0.68
OCD	Adrenal_Pancreas	4.12	1.70	7.08E-08	1.05E-07	0.67
Anxiety disorders	Hematopoietic	5.44	3.15	2.70E-08	4.92E-08	0.55
Anorexia nervosa	Kidney	1.16	2.87	5.40E-08	1.03E-07	0.52
Autism spectrum disorder	SkeletalMuscle	1.86	0.86	4.54E-08	9.05E-08	0.50
Anorexia nervosa	CNS	0.99	1.00	2.10E-08	4.96E-08	0.42
Autism spectrum disorder	Adrenal_Pancreas	1.90	0.99	3.08E-08	9.76E-08	0.32
Bipolar disorder	SkeletalMuscle	2.96	0.42	6.97E-09	2.97E-08	0.23
Anorexia nervosa	GI	0.51	1.13	1.14E-08	5.64E-08	0.20
OCD	SkeletalMuscle	3.27	1.50	1.63E-08	8.92E-08	0.18
Autism spectrum disorder	Connective_Bone	1.36	0.72	2.82E-09	7.87E-08	0.04
Tourette Syndrome	Liver	1.60	1.26	2.49E-09	7.77E-08	0.03
Anorexia nervosa	Adrenal_Pancreas	1.19	1.87	1.50E-09	8.28E-08	0.02
Anorexia nervosa	SkeletalMuscle	0.90	1.50	-1.88E-09	6.85E-08	-0.03
Autism spectrum disorder	Hematopoietic	1.46	0.48	-3.43E-09	6.75E-08	-0.05
Major depressive disorder	Hematopoietic	1.07	0.24	-3.96E-10	4.25E-09	-0.09
Anorexia nervosa	Hematopoietic	-0.09	0.87	-5.42E-09	5.77E-08	-0.09
Anorexia nervosa	Other	0.88	0.98	-8.19E-09	5.51E-08	-0.15
OCD	Other	1.40	1.08	-1.32E-08	8.03E-08	-0.16

Anorexia nervosa	Connective_Bone	0.04	1.29	-1.08E-08	5.79E-08	-0.19
ADHD	Cardiovascular	0.42	1.10	-2.55E-09	1.19E-08	-0.21
OCD	Cardiovascular	2.89	1.56	-4.71E-08	9.27E-08	-0.51
OCD	Liver	2.74	1.74	-4.50E-08	8.65E-08	-0.52
ADHD	Hematopoietic	0.33	0.58	-4.79E-09	8.19E-09	-0.58
Schizophrenia	SkeletalMuscle	2.26	0.27	-1.58E-08	2.58E-08	-0.61
Anorexia nervosa	Liver	-0.19	1.69	-4.00E-08	6.18E-08	-0.65
ADHD	Other	0.17	0.71	-6.21E-09	9.15E-09	-0.68
Autism spectrum disorder	GI	1.43	0.69	-5.52E-08	7.86E-08	-0.70
Bipolar disorder	Connective_Bone	2.33	0.36	-1.87E-08	2.43E-08	-0.77
ADHD	Liver	0.19	1.22	-7.28E-09	9.42E-09	-0.77
Major depressive disorder	SkeletalMuscle	2.09	0.41	-4.02E-09	5.01E-09	-0.80
Anxiety disorders	Cardiovascular	6.90	4.65	-5.47E-08	6.53E-08	-0.84
OCD	Hematopoietic	0.21	0.93	-7.39E-08	8.44E-08	-0.87
Tourette Syndrome	Connective_Bone	1.09	0.99	-6.87E-08	7.07E-08	-0.97
Anxiety disorders	Other	3.90	3.00	-5.13E-08	5.12E-08	-1.00
ADHD	Connective_Bone	-0.02	0.96	-8.75E-09	8.65E-09	-1.01
Major depressive disorder	Kidney	2.15	0.68	-8.00E-09	7.35E-09	-1.09
Tourette Syndrome	GI	1.39	0.76	-7.42E-08	6.33E-08	-1.17
Tourette Syndrome	Other	1.18	0.72	-8.30E-08	7.00E-08	-1.19
Schizophrenia	Connective_Bone	1.80	0.25	-2.70E-08	2.27E-08	-1.19
OCD	Connective_Bone	1.19	1.29	-9.69E-08	7.66E-08	-1.27
Bipolar disorder	Liver	2.39	0.53	-3.80E-08	2.81E-08	-1.35
Tourette Syndrome	Cardiovascular	1.15	1.18	-1.21E-07	8.65E-08	-1.40
Autism spectrum disorder	Cardiovascular	1.35	0.92	-1.46E-07	1.02E-07	-1.43
ADHD	Kidney	-1.33	1.95	-2.25E-08	1.56E-08	-1.45
ADHD	Adrenal_Pancreas	-0.45	1.21	-1.56E-08	1.04E-08	-1.49
Anorexia nervosa	Cardiovascular	0.44	1.55	-1.03E-07	6.70E-08	-1.54
Tourette Syndrome	Kidney	-0.69	2.09	-1.76E-07	1.12E-07	-1.57
Schizophrenia	Liver	1.86	0.30	-4.14E-08	2.33E-08	-1.78
Major depressive disorder	Other	1.31	0.29	-8.82E-09	4.56E-09	-1.93
Anxiety disorders	SkeletalMuscle	4.23	4.48	-1.08E-07	5.52E-08	-1.96
Anxiety disorders	Adrenal_Pancreas	2.13	5.00	-1.33E-07	6.48E-08	-2.06
Anxiety disorders	Liver	2.73	4.89	-1.22E-07	5.82E-08	-2.09
Schizophrenia	Cardiovascular	2.13	0.28	-6.25E-08	2.88E-08	-2.17
Major depressive disorder	Liver	1.40	0.49	-1.20E-08	5.50E-09	-2.18
Bipolar disorder	Cardiovascular	2.37	0.43	-7.04E-08	3.05E-08	-2.31
Anxiety disorders	Kidney	1.76	7.29	-1.86E-07	7.96E-08	-2.34
Bipolar disorder	Kidney	2.04	0.79	-9.80E-08	4.00E-08	-2.45
ADHD	GI	-0.64	0.78	-1.93E-08	7.83E-09	-2.46
Bipolar disorder	Other	1.75	0.28	-6.08E-08	2.44E-08	-2.50
Bipolar disorder	GI	1.66	0.29	-6.83E-08	2.29E-08	-2.98
Major depressive disorder	Cardiovascular	1.81	0.48	-1.94E-08	6.09E-09	-3.19
Anxiety disorders	GI	-0.12	3.60	-1.83E-07	5.37E-08	-3.41
Schizophrenia	Other	1.31	0.17	-9.80E-08	2.37E-08	-4.13
Schizophrenia	Kidney	1.16	0.43	-1.40E-07	3.16E-08	-4.42
Schizophrenia	GI	1.15	0.20	-1.10E-07	2.45E-08	-4.51

Major depressive disorder	GI	0.74	0.31	-2.12E-08	4.33E-09	-4.89

lers, behavioral-cognitive phenotypes, and additional traits.

Neurological disorders

Phenotype	Tissue	Enrichment	SE	Coeff.	SE	Coeff. z-score
Multiple sclerosis	Hematopoietic	4.90	0.54	2.85E-07	5.44E-08	**5.24**
Generalized epilepsy	CNS	2.79	0.60	1.68E-07	4.34E-08	**3.87**
Migraine without aura	Kidney	8.80	2.14	2.96E-08	1.09E-08	2.72
Early-onset stroke	SkeletalMuscle	6.71	2.86	1.65E-07	6.49E-08	2.55
Epilepsy	CNS	2.47	1.01	6.62E-08	2.62E-08	2.53
Migraine	CNS	3.39	0.30	7.64E-09	3.25E-09	2.35
Alzheimer's disease	Liver	8.32	2.02	4.29E-08	2.01E-08	2.13
Alzheimer's disease	Hematopoietic	5.13	0.91	3.68E-08	1.76E-08	2.10
Migraine	Cardiovascular	4.30	0.51	9.58E-09	4.74E-09	2.02
Focal epilepsy	Cardiovascular	2.47	3.34	9.19E-08	4.55E-08	2.02
Migraine	Kidney	5.61	0.95	1.49E-08	7.83E-09	1.91
Intracerebral hemorrhage	Cardiovascular	9.75	7.68	6.35E-07	3.52E-07	1.81
Migraine with aura	SkeletalMuscle	6.80	1.67	1.24E-08	7.21E-09	1.72
Alzheimer's disease	Other	4.27	0.97	2.86E-08	1.67E-08	1.71
Migraine with aura	Cardiovascular	6.76	1.80	1.22E-08	7.24E-09	1.69
Migraine with aura	Kidney	10.13	2.99	1.69E-08	1.02E-08	1.65
Epilepsy	Hematopoietic	1.42	0.83	3.84E-08	2.62E-08	1.46
Migraine without aura	GI	4.00	0.91	8.59E-09	6.03E-09	1.42
Generalized epilepsy	Hematopoietic	1.52	0.53	6.48E-08	4.59E-08	1.41
Migraine without aura	Connective_Bone	4.70	1.09	8.79E-09	6.41E-09	1.37
Migraine	SkeletalMuscle	4.08	0.47	6.31E-09	4.78E-09	1.32
Migraine with aura	Adrenal_Pancreas	6.71	1.97	9.82E-09	7.56E-09	1.30
Parkinson's disease	CNS	3.85	0.79	9.66E-08	7.58E-08	1.28
Migraine with aura	Hematopoietic	2.68	0.84	7.38E-09	5.81E-09	1.27
Ischemic stroke	Cardiovascular	4.80	1.85	4.04E-08	3.21E-08	1.26
Early-onset stroke	Cardiovascular	4.61	2.92	9.05E-08	7.28E-08	1.24
Focal epilepsy	Hematopoietic	-0.36	2.07	3.45E-08	2.96E-08	1.16
Migraine	Connective_Bone	3.70	0.46	5.22E-09	4.60E-09	1.13
Generalized epilepsy	Adrenal_Pancreas	1.97	1.03	6.56E-08	5.80E-08	1.13
Alzheimer's disease	CNS	4.91	1.12	1.54E-08	1.37E-08	1.12
Migraine without aura	Cardiovascular	4.92	1.32	9.49E-09	8.50E-09	1.12
Parkinson's disease	Adrenal_Pancreas	4.91	1.49	9.06E-08	8.22E-08	1.10
Focal epilepsy	Liver	1.16	3.70	4.44E-08	4.15E-08	1.07
Ischemic stroke	SkeletalMuscle	4.04	1.62	2.79E-08	2.88E-08	0.97
Epilepsy	Cardiovascular	3.33	1.53	3.66E-08	4.10E-08	0.89
Migraine	GI	2.96	0.35	3.45E-09	4.00E-09	0.86
Migraine	Liver	3.78	0.56	4.32E-09	5.12E-09	0.84
Migraine with aura	CNS	4.24	1.15	4.05E-09	4.88E-09	0.83
Ischemic stroke	Connective_Bone	3.72	1.47	2.24E-08	2.73E-08	0.82
Parkinson's disease	Hematopoietic	2.63	0.89	4.23E-08	5.28E-08	0.80
Early-onset stroke	Adrenal_Pancreas	3.88	2.96	4.81E-08	6.63E-08	0.73
Focal epilepsy	CNS	-2.08	2.76	2.16E-08	2.98E-08	0.72

Early-onset stroke	Liver	3.05	3.05	4.44E-08	6.49E-08	0.68
Epilepsy	Liver	2.52	1.63	2.10E-08	3.60E-08	0.58
Migraine without aura	CNS	3.62	0.75	2.84E-09	5.19E-09	0.55
Early-onset stroke	CNS	1.94	1.92	2.27E-08	4.20E-08	0.54
Migraine	Adrenal_Pancreas	3.75	0.50	2.25E-09	4.43E-09	0.51
Intracerebral hemorrhage	GI	4.40	4.35	1.25E-07	2.55E-07	0.49
Early-onset stroke	Hematopoietic	0.52	1.57	2.58E-08	5.42E-08	0.48
Ischemic stroke	Other	2.86	1.15	1.21E-08	2.55E-08	0.47
Alzheimer's disease	Connective_Bone	5.02	1.41	8.91E-09	2.00E-08	0.44
Intracerebral hemorrhage	Other	3.57	3.77	9.92E-08	2.37E-07	0.42
Generalized epilepsy	Other	1.44	0.64	2.27E-08	5.46E-08	0.42
Migraine without aura	Adrenal_Pancreas	4.25	1.26	3.15E-09	7.91E-09	0.40
Intracerebral hemorrhage	CNS	3.65	3.78	8.30E-08	2.17E-07	0.38
Epilepsy	Adrenal_Pancreas	2.35	1.48	1.42E-08	3.76E-08	0.38
Intracerebral hemorrhage	Kidney	7.97	9.75	1.64E-07	4.38E-07	0.37
Focal epilepsy	Kidney	-1.64	5.06	1.95E-08	5.56E-08	0.35
Ischemic stroke	Hematopoietic	1.43	0.84	8.52E-09	2.47E-08	0.35
Alzheimer's disease	Kidney	8.69	3.00	7.52E-09	3.00E-08	0.25
Alzheimer's disease	Adrenal_Pancreas	5.50	1.70	5.06E-09	2.19E-08	0.23
Ischemic stroke	CNS	1.87	1.07	4.38E-09	1.99E-08	0.22
Alzheimer's disease	GI	4.11	1.06	3.59E-09	1.77E-08	0.20
Migraine	Hematopoietic	1.96	0.24	7.27E-10	3.65E-09	0.20
Alzheimer's disease	SkeletalMuscle	5.05	1.53	4.23E-09	2.19E-08	0.19
Migraine with aura	GI	3.59	1.18	8.23E-10	6.66E-09	0.12
Generalized epilepsy	SkeletalMuscle	1.39	0.88	5.46E-09	5.68E-08	0.10
Migraine with aura	Connective_Bone	4.37	1.46	5.42E-10	5.99E-09	0.09
Ischemic stroke	Liver	2.57	2.00	6.24E-10	3.06E-08	0.02
Early-onset stroke	Kidney	1.75	4.46	-2.37E-09	8.56E-08	-0.03
Early-onset stroke	Connective_Bone	1.67	2.37	-3.65E-09	5.70E-08	-0.06
Migraine with aura	Other	3.51	1.10	-5.64E-10	5.59E-09	-0.10
Migraine with aura	Liver	4.41	1.91	-1.19E-09	7.01E-09	-0.17
Generalized epilepsy	GI	1.12	0.67	-1.14E-08	5.35E-08	-0.21
Ischemic stroke	Adrenal_Pancreas	2.65	1.89	-1.04E-08	3.42E-08	-0.30
Parkinson's disease	Connective_Bone	3.12	1.88	-2.37E-08	7.62E-08	-0.31
Early-onset stroke	GI	0.73	2.30	-1.89E-08	5.68E-08	-0.33
Migraine	Other	2.70	0.29	-1.36E-09	3.99E-09	-0.34
Epilepsy	Kidney	1.83	2.25	-1.86E-08	5.09E-08	-0.37
Parkinson's disease	SkeletalMuscle	3.17	1.12	-3.55E-08	9.56E-08	-0.37
Parkinson's disease	Liver	3.55	1.41	-2.69E-08	6.93E-08	-0.39
Multiple sclerosis	SkeletalMuscle	4.10	0.77	-2.70E-08	5.85E-08	-0.46
Focal epilepsy	Adrenal_Pancreas	-3.19	3.94	-2.14E-08	4.61E-08	-0.47
Focal epilepsy	SkeletalMuscle	-3.35	4.05	-2.01E-08	4.28E-08	-0.47
Intracerebral hemorrhage	SkeletalMuscle	1.92	5.46	-1.52E-07	2.91E-07	-0.52
Migraine without aura	Liver	3.23	1.26	-3.71E-09	6.87E-09	-0.54
Migraine without aura	Other	2.84	0.79	-3.78E-09	6.78E-09	-0.56
Ischemic stroke	Kidney	1.55	2.88	-2.24E-08	3.87E-08	-0.58
Generalized epilepsy	Liver	0.61	1.01	-4.10E-08	6.53E-08	-0.63

Migraine without aura	Hematopoietic	2.36	0.63	-3.98E-09	6.21E-09	-0.64
Multiple sclerosis	Connective_Bone	3.73	0.71	-3.96E-08	6.08E-08	-0.65
Intracerebral hemorrhage	Connective_Bone	1.01	4.21	-1.51E-07	2.28E-07	-0.66
Parkinson's disease	Other	2.44	0.88	-3.87E-08	5.73E-08	-0.68
Early-onset stroke	Other	1.13	1.99	-3.53E-08	5.21E-08	-0.68
Generalized epilepsy	Connective_Bone	1.06	0.81	-3.46E-08	5.04E-08	-0.69
Migraine without aura	SkeletalMuscle	3.49	1.08	-5.11E-09	7.07E-09	-0.72
Focal epilepsy	Other	-2.66	2.67	-2.85E-08	3.72E-08	-0.77
Epilepsy	SkeletalMuscle	1.11	1.50	-2.77E-08	3.58E-08	-0.77
Ischemic stroke	GI	1.74	1.28	-2.03E-08	2.53E-08	-0.80
Multiple sclerosis	Adrenal_Pancreas	4.12	0.87	-5.48E-08	6.47E-08	-0.85
Intracerebral hemorrhage	Hematopoietic	1.40	2.75	-2.01E-07	2.27E-07	-0.88
Epilepsy	Connective_Bone	0.39	1.27	-3.02E-08	3.30E-08	-0.92
Parkinson's disease	GI	2.16	1.03	-5.20E-08	5.54E-08	-0.94
Multiple sclerosis	Kidney	5.86	1.39	-9.33E-08	8.70E-08	-1.07
Multiple sclerosis	CNS	2.75	0.50	-4.63E-08	4.17E-08	-1.11
Generalized epilepsy	Cardiovascular	0.71	0.99	-7.58E-08	6.50E-08	-1.17
Multiple sclerosis	Liver	4.33	0.93	-7.94E-08	6.01E-08	-1.32
Focal epilepsy	Connective_Bone	-5.31	3.73	-5.58E-08	3.46E-08	-1.61
Epilepsy	Other	0.24	0.95	-5.10E-08	2.98E-08	-1.71
Generalized epilepsy	Kidney	-0.84	1.57	-1.42E-07	8.14E-08	-1.75
Focal epilepsy	GI	-3.88	3.41	-6.58E-08	3.36E-08	-1.96
Alzheimer's disease	Cardiovascular	2.19	1.40	-4.47E-08	2.20E-08	-2.03
Intracerebral hemorrhage	Adrenal_Pancreas	-3.56	6.51	-6.66E-07	3.28E-07	-2.03
Multiple sclerosis	Cardiovascular	3.34	0.84	-1.38E-07	6.60E-08	-2.09
Parkinson's disease	Cardiovascular	1.74	1.55	-1.48E-07	6.90E-08	-2.15
Epilepsy	GI	-0.10	1.11	-7.08E-08	3.27E-08	-2.17
Intracerebral hemorrhage	Liver	-5.46	6.90	-7.03E-07	2.96E-07	-2.37
Parkinson's disease	Kidney	1.23	2.44	-2.18E-07	9.15E-08	-2.38
Multiple sclerosis	Other	2.24	0.51	-1.38E-07	5.35E-08	-2.57
Multiple sclerosis	GI	2.32	0.57	-1.96E-07	5.77E-08	-3.40

Behavioral-cognitive phenotypes and additional traits

Phenotype	Tissue	Enrichment	SE
Years of education	CNS	2.87	0.19
Intelligence	CNS	3.41	0.32
Height	Connective_Bone	5.32	0.38
BMI	CNS	2.67	0.18
Crohn's disease	Hematopoietic	4.19	0.43
Neuroticism	CNS	2.47	0.29
College attainment	CNS	3.31	0.45
Height	Cardiovascular	4.23	0.38
Height	Other	3.42	0.21
Depressive symptoms	Adrenal_Pancreas	5.15	0.94
Never/ever smoked	CNS	3.45	0.73
BMI	Adrenal_Pancreas	2.92	0.28
Height	SkeletalMuscle	4.06	0.33
Depressive symptoms	CNS	2.84	0.49
Intelligence	Adrenal_Pancreas	3.28	0.51
BMI	Hematopoietic	1.63	0.14
Coronary artery disease	Liver	4.57	1.00
Cognitive performance	Liver	3.85	1.81
Openness	CNS	4.84	1.82
Subjective well-being	CNS	3.33	0.52
Height	GI	3.04	0.23
Openness	Hematopoietic	3.49	1.46
Depressive symptoms	Kidney	5.42	1.30
Conscientiousness	GI	6.46	2.63
Coronary artery disease	Other	3.41	0.57
Intelligence	SkeletalMuscle	2.92	0.46
Depressive symptoms	Hematopoietic	1.70	0.38
Cognitive performance	Adrenal_Pancreas	3.44	1.76
Coronary artery disease	Kidney	5.90	1.62
Cognitive performance	CNS	2.42	1.00
Years of education	Adrenal_Pancreas	2.61	0.36
Cigarettes per day	Connective_Bone	2.95	1.50
Extraversion	SkeletalMuscle	4.26	1.39
Conscientiousness	SkeletalMuscle	7.72	3.08
Coronary artery disease	Cardiovascular	4.28	0.93
Cognitive performance	Cardiovascular	2.52	1.50
Subjective well-being	Hematopoietic	2.36	0.36
Extraversion	CNS	3.27	0.92
Height	Kidney	4.45	0.65
Coronary artery disease	Connective_Bone	3.89	0.78
Cognitive performance	Kidney	3.37	2.70
Years of education	Hematopoietic	1.45	0.15

Coronary artery disease	SkeletalMuscle	4.20	0.85
Never/ever smoked	Adrenal_Pancreas	3.60	1.12
Cigarettes per day	Adrenal_Pancreas	3.28	1.90
Subjective well-being	Adrenal_Pancreas	3.24	0.81
Depressive symptoms	Liver	3.26	0.91
Height	Liver	3.65	0.36
Cognitive performance	Hematopoietic	1.95	0.86
Coronary artery disease	GI	2.94	0.60
College attainment	Liver	3.01	0.75
BMI	SkeletalMuscle	2.26	0.25
Extraversion	Cardiovascular	3.82	1.42
Cigarettes per day	CNS	1.68	1.20
Coronary artery disease	Hematopoietic	2.18	0.44
Coronary artery disease	Adrenal_Pancreas	3.67	0.98
Extraversion	Adrenal_Pancreas	3.57	1.38
Conscientiousness	Kidney	9.92	5.61
Height	Adrenal_Pancreas	3.44	0.44
Cigarettes per day	GI	1.92	1.53
Height	Hematopoietic	2.20	0.21
College attainment	Hematopoietic	1.40	0.37
Conscientiousness	Adrenal_Pancreas	5.68	3.60
Never/ever smoked	Liver	2.52	1.14
BMI	Connective_Bone	1.89	0.24
Intelligence	Liver	2.00	0.50
Cigarettes per day	Liver	1.10	2.35
Openness	SkeletalMuscle	3.75	2.12
Cigarettes per day	Other	1.39	1.45
Extraversion	Connective_Bone	2.76	1.09
Conscientiousness	Liver	4.80	3.03
Neuroticism	Hematopoietic	1.18	0.30
College attainment	SkeletalMuscle	2.84	0.67
Cigarettes per day	Hematopoietic	1.18	1.00
College attainment	Connective_Bone	2.15	0.53
Never/ever smoked	SkeletalMuscle	2.48	1.01
Conscientiousness	Other	2.95	1.96
Crohn's disease	Kidney	5.13	1.26
Conscientiousness	CNS	3.15	2.04
Intelligence	Other	1.85	0.30
Extraversion	Other	2.38	0.95
Cognitive performance	Connective_Bone	0.99	1.23
Subjective well-being	Cardiovascular	2.47	0.73
Crohn's disease	SkeletalMuscle	3.71	0.69
Never/ever smoked	Connective_Bone	1.76	0.87
Conscientiousness	Cardiovascular	5.61	3.10
Neuroticism	Adrenal_Pancreas	1.71	0.44
Cigarettes per day	SkeletalMuscle	0.91	2.14
Openness	Kidney	3.45	4.23

Conscientiousness	Hematopoietic	2.02	1.56
Cognitive performance	SkeletalMuscle	0.72	1.47
College attainment	Adrenal_Pancreas	2.60	0.75
College attainment	Cardiovascular	3.05	0.72
Years of education	Liver	1.90	0.29
Crohn's disease	Liver	3.99	0.76
Years of education	SkeletalMuscle	2.08	0.25
Neuroticism	Liver	1.35	0.56
Subjective well-being	SkeletalMuscle	2.29	0.67
Subjective well-being	Liver	2.20	0.79
Extraversion	Hematopoietic	1.68	0.84
Subjective well-being	Other	1.99	0.42
Cognitive performance	GI	1.11	1.03
Openness	Liver	1.66	2.30
Cognitive performance	Other	0.98	1.00
Extraversion	GI	2.12	0.96
Never/ever smoked	Hematopoietic	1.16	0.53
Openness	Adrenal_Pancreas	2.19	2.33
Intelligence	Kidney	1.73	0.78
Conscientiousness	Connective_Bone	1.81	2.24
Subjective well-being	Kidney	2.04	1.32
Depressive symptoms	SkeletalMuscle	2.15	0.73
Crohn's disease	Connective_Bone	3.22	0.67
Subjective well-being	Connective_Bone	2.07	0.56
Intelligence	Hematopoietic	1.35	0.21
Never/ever smoked	Kidney	1.19	1.84
Extraversion	Kidney	0.72	2.39
Openness	Cardiovascular	2.75	2.23
Coronary artery disease	CNS	2.35	0.54
College attainment	Kidney	2.17	1.12
Crohn's disease	GI	2.92	0.53
Never/ever smoked	Other	1.66	0.67
Cigarettes per day	Kidney	-1.99	3.01
BMI	Liver	1.85	0.30
Openness	Connective_Bone	1.07	1.76
Never/ever smoked	Cardiovascular	2.53	1.01
College attainment	Other	1.74	0.45
Neuroticism	SkeletalMuscle	1.45	0.41
Neuroticism	Kidney	0.81	0.66
Intelligence	Cardiovascular	2.28	0.49
Cigarettes per day	Cardiovascular	-0.18	2.41
Years of education	Connective_Bone	1.64	0.22
Years of education	Cardiovascular	2.15	0.31
Crohn's disease	Other	2.29	0.48
Depressive symptoms	Connective_Bone	1.24	0.61
Extraversion	Liver	0.78	1.57
Depressive symptoms	Other	1.19	0.48

Never/ever smoked	GI	1.19	0.73
BMI	Kidney	2.01	0.45
Depressive symptoms	GI	1.36	0.51
Neuroticism	Other	1.20	0.32
College attainment	GI	1.53	0.45
Openness	GI	0.81	1.40
Intelligence	Connective_Bone	1.46	0.37
Neuroticism	Connective_Bone	0.85	0.37
Depressive symptoms	Cardiovascular	2.22	0.74
Crohn's disease	Cardiovascular	2.64	0.63
Crohn's disease	CNS	2.15	0.51
BMI	Other	1.43	0.16
Crohn's disease	Adrenal_Pancreas	2.85	0.72
BMI	Cardiovascular	1.80	0.27
Openness	Other	-0.60	1.48
Subjective well-being	GI	1.47	0.47
Neuroticism	GI	0.87	0.33
Years of education	Kidney	1.36	0.43
Height	CNS	2.41	0.22
Neuroticism	Cardiovascular	1.26	0.48
Years of education	Other	1.35	0.17
BMI	GI	1.33	0.19
Intelligence	GI	1.17	0.35
Years of education	GI	1.24	0.19

Coeff.	SE	Coeff. z-score
9.51E-08	1.15E-08	**8.29**
8.30E-08	1.23E-08	**6.73**
2.24E-07	3.55E-08	**6.32**
2.73E-08	4.46E-09	**6.13**
3.60E-07	6.66E-08	**5.41**
3.83E-08	8.45E-09	**4.53**
2.71E-08	6.52E-09	**4.16**
1.28E-07	3.08E-08	**4.15**
8.26E-08	2.19E-08	**3.78**
3.77E-08	1.04E-08	**3.62**
3.06E-08	9.13E-09	**3.35**
2.15E-08	6.69E-09	3.21
7.76E-08	2.65E-08	2.93
1.68E-08	6.05E-09	2.78
4.96E-08	1.96E-08	2.53
1.14E-08	4.62E-09	2.46
3.25E-08	1.43E-08	2.28
1.23E-07	5.42E-08	2.27
8.15E-08	3.61E-08	2.26
1.57E-08	7.13E-09	2.20
4.87E-08	2.24E-08	2.17
8.40E-08	4.18E-08	2.01
2.53E-08	1.26E-08	2.01
9.64E-08	4.89E-08	1.97
2.52E-08	1.32E-08	1.91
3.55E-08	1.97E-08	1.81
1.24E-08	6.93E-09	1.80
1.11E-07	6.34E-08	1.75
4.22E-08	2.48E-08	1.71
5.98E-08	3.58E-08	1.67
3.60E-08	2.25E-08	1.60
3.13E-08	2.02E-08	1.55
2.44E-08	1.59E-08	1.54
9.12E-08	6.07E-08	1.50
3.03E-08	2.03E-08	1.50
7.82E-08	5.44E-08	1.44
9.68E-09	6.75E-09	1.43
1.46E-08	1.04E-08	1.40
5.49E-08	4.14E-08	1.33
1.68E-08	1.41E-08	1.19
1.00E-07	8.48E-08	1.18
1.63E-08	1.40E-08	1.16

Key:
CNS
Connective_Bone
Hematopoietic
Cardiovascular
Other
Adrenal_Pancreas
SkeletalMuscle
Liver
GI
Kidney

For exact makeup of categories, see
H. K. Finucane et al., Partitioning heritability by function

1.86E-08	1.64E-08	1.13
1.50E-08	1.35E-08	1.11
2.87E-08	2.61E-08	1.10
1.01E-08	9.58E-09	1.06
8.96E-09	8.76E-09	1.02
2.38E-08	2.47E-08	0.96
3.85E-08	4.50E-08	0.86
1.04E-08	1.31E-08	0.80
6.78E-09	9.08E-09	0.75
4.44E-09	6.15E-09	0.72
1.32E-08	1.85E-08	0.71
1.23E-08	1.75E-08	0.71
7.71E-09	1.24E-08	0.62
9.94E-09	1.66E-08	0.60
1.03E-08	1.82E-08	0.57
4.98E-08	8.89E-08	0.56
1.24E-08	3.18E-08	0.39
8.11E-09	2.25E-08	0.36
7.25E-09	2.33E-08	0.31
2.50E-09	8.31E-09	0.30
1.88E-08	7.49E-08	0.25
2.02E-09	1.24E-08	0.16
3.25E-10	5.40E-09	0.06
1.03E-09	1.72E-08	0.06
1.40E-09	2.67E-08	0.05
6.73E-10	4.81E-08	0.01
-1.48E-10	2.20E-08	-0.01
-5.26E-10	1.36E-08	-0.04
-1.96E-09	4.62E-08	-0.04
-6.31E-10	9.35E-09	-0.07
-1.09E-09	9.04E-09	-0.12
-2.73E-09	2.15E-08	-0.13
-1.08E-09	8.28E-09	-0.13
-2.63E-09	1.45E-08	-0.18
-1.28E-08	5.32E-08	-0.24
-3.25E-08	1.26E-07	-0.26
-1.13E-08	3.91E-08	-0.29
-4.80E-09	1.62E-08	-0.30
-4.43E-09	1.36E-08	-0.33
-1.52E-08	4.59E-08	-0.33
-3.75E-09	1.05E-08	-0.36
-2.77E-08	7.71E-08	-0.36
-4.49E-09	1.21E-08	-0.37
-2.18E-08	5.71E-08	-0.38
-5.46E-09	1.38E-08	-0.40
-1.01E-08	2.48E-08	-0.41
-3.65E-08	8.73E-08	-0.42

-1.95E-08	4.67E-08	-0.42
-2.53E-08	5.74E-08	-0.44
-5.03E-09	1.08E-08	-0.47
-5.55E-09	1.11E-08	-0.50
-7.74E-09	1.49E-08	-0.52
-3.89E-08	6.97E-08	-0.56
-8.79E-09	1.53E-08	-0.57
-6.22E-09	1.08E-08	-0.58
-5.25E-09	8.98E-09	-0.58
-5.17E-09	8.45E-09	-0.61
-9.13E-09	1.41E-08	-0.65
-5.44E-09	8.21E-09	-0.66
-2.92E-08	4.33E-08	-0.68
-3.65E-08	5.27E-08	-0.69
-3.53E-08	4.80E-08	-0.74
-1.06E-08	1.36E-08	-0.78
-9.52E-09	1.18E-08	-0.81
-5.07E-08	5.76E-08	-0.88
-2.22E-08	2.41E-08	-0.92
-4.46E-08	4.76E-08	-0.94
-1.33E-08	1.36E-08	-0.97
-8.46E-09	8.59E-09	-0.98
-8.06E-08	8.19E-08	-0.98
-7.34E-09	7.45E-09	-0.99
-1.38E-08	1.31E-08	-1.05
-2.03E-08	1.90E-08	-1.07
-2.44E-08	2.26E-08	-1.08
-6.27E-08	5.69E-08	-1.10
-1.21E-08	1.08E-08	-1.12
-1.45E-08	1.26E-08	-1.15
-7.72E-08	6.65E-08	-1.16
-1.43E-08	1.23E-08	-1.16
-3.69E-08	3.11E-08	-1.19
-6.84E-09	5.57E-09	-1.23
-5.51E-08	4.39E-08	-1.26
-2.09E-08	1.55E-08	-1.34
-1.16E-08	8.44E-09	-1.37
-1.60E-08	1.16E-08	-1.38
-2.37E-08	1.69E-08	-1.40
-2.76E-08	1.94E-08	-1.42
-4.24E-08	2.86E-08	-1.49
-1.94E-08	1.29E-08	-1.50
-2.85E-08	1.90E-08	-1.50
-1.24E-07	8.14E-08	-1.52
-1.24E-08	7.60E-09	-1.64
-2.47E-08	1.49E-08	-1.66
-1.30E-08	7.34E-09	-1.77

-2.10E-08	1.16E-08	-1.81
-1.31E-08	6.99E-09	-1.87
-1.27E-08	6.68E-09	-1.91
-1.70E-08	8.82E-09	-1.93
-1.50E-08	7.54E-09	-2.00
-8.96E-08	4.38E-08	-2.04
-3.18E-08	1.47E-08	-2.17
-2.58E-08	1.12E-08	-2.30
-2.17E-08	9.38E-09	-2.31
-2.07E-07	8.91E-08	-2.33
-1.50E-07	6.09E-08	-2.45
-1.22E-08	4.77E-09	-2.56
-1.93E-07	7.38E-08	-2.62
-1.73E-08	6.44E-09	-2.68
-1.27E-07	4.50E-08	-2.81
-2.11E-08	7.31E-09	-2.89
-3.23E-08	9.97E-09	-3.24
-6.92E-08	2.02E-08	-3.43
-5.91E-08	1.71E-08	-3.46
-3.89E-08	1.10E-08	-3.53
-4.72E-08	1.32E-08	-3.58
-1.75E-08	4.70E-09	-3.73
-5.86E-08	1.56E-08	-3.76
-5.67E-08	1.26E-08	-4.49

al annotation using genome-wide association summary statistics. Nat Genet. 2015 Nov; 47(11): 1228–12

:35.

Supplementary Table 13: Data sources, responsible consortia, and data a

Data sources (valid as of 8/2/18)

Disorder or phenotype (reference)
Psychiatric disorders
ADHD
Anorexia nervosa(68)
Anxiety disorder(69)
Autism spectrum disorders(70)
Bipolar disorder
Major depressive disorder
OCD – PGC
PTSD – PGC
Schizophrenia(22)
Tourette Syndrome
Neurological disorders
Alzheimer's disease(18)
Epilepsy and subtypes, focal and generalized(71)
Intracerebral hemorrhage(72)
Ischemic stroke and subtypes (cardioembolic, early onset, small vessel and large vessel)(73)
Migraine and subtypes, migraine with and without aura
Multiple sclerosis(74)
Parkinson's disease(21)
Behavioral-cognitive phenotypes
College attainment, years of education(75)
Childhood cognitive performance(76)
Extraversion, agreeableness, conscientiousness and openness (27)
IQ(77)
Neuroticism, depressive symptoms and subjective well-being(78)
Never/ever smoked, cigarettes per day(79)
Additional phenotypes
BMI(63)
Height(80)
Crohn’s disease(81)
Coronary artery disease(82)
Genotype data used for simulations and power analyses
UK Biobank

vailability

Consortium or dataset identifier	Availability
PGC-ADD2	Freely available
PGC-ED	Freely available
ANGST	Freely available
PGC-AUT	Freely available
PGC-BIP2	By application, later freely available
PGC-MDD2	By application, later freely available
PGC-TSOCD	Freely available
PGC-PTSD	Freely available
PGC-SCZ2	Freely available
PGC-TSOCD	By application
IGAP	Freely available
ILAE	Freely available
ISGC	Freely available (PMC3980413)
METASTROKE dataset of the ISGC	Freely available (PMC3490334)
IHGC	By application
IMSGC	By application
IPDGC	By application
SSGAC	Freely available
SSGAC	Freely available
GPC	Freely available
CTG	Freely available
SSGAC	Freely available
TAG	Freely available
GIANT	Freely available
GIANT	Freely available
IIBDGC	Freely available
CARDIoGRAM	Freely available
UK Biobank	Available through application

Address

http://www.med.unc.edu/pgc/results-and-downloads
http://www.med.unc.edu/pgc/results-and-downloads
http://www.med.unc.edu/pgc/results-and-downloads
http://www.med.unc.edu/pgc/results-and-downloads
http://www.med.unc.edu/pgc/results-and-downloads
http://www.med.unc.edu/pgc/results-and-downloads
http://www.med.unc.edu/pgc/results-and-downloads
http://www.med.unc.edu/pgc/results-and-downloads
http://www.med.unc.edu/pgc/results-and-downloads
http://www.med.unc.edu/pgc/pgc-workgroups

---

http://web.pasteur-lille.fr/en/recherche/u744/igap/igap_download.php
http://www.epigad.org/gwas_ilae2014/
http://cerebrovascularportal.org/informational/downloads
http://cerebrovascularportal.org/informational/downloads
http://www.headachegenetics.org/content/datasets-and-cohorts
http://imsgenetics.org/?page_id=83
www.pdgene.org

---

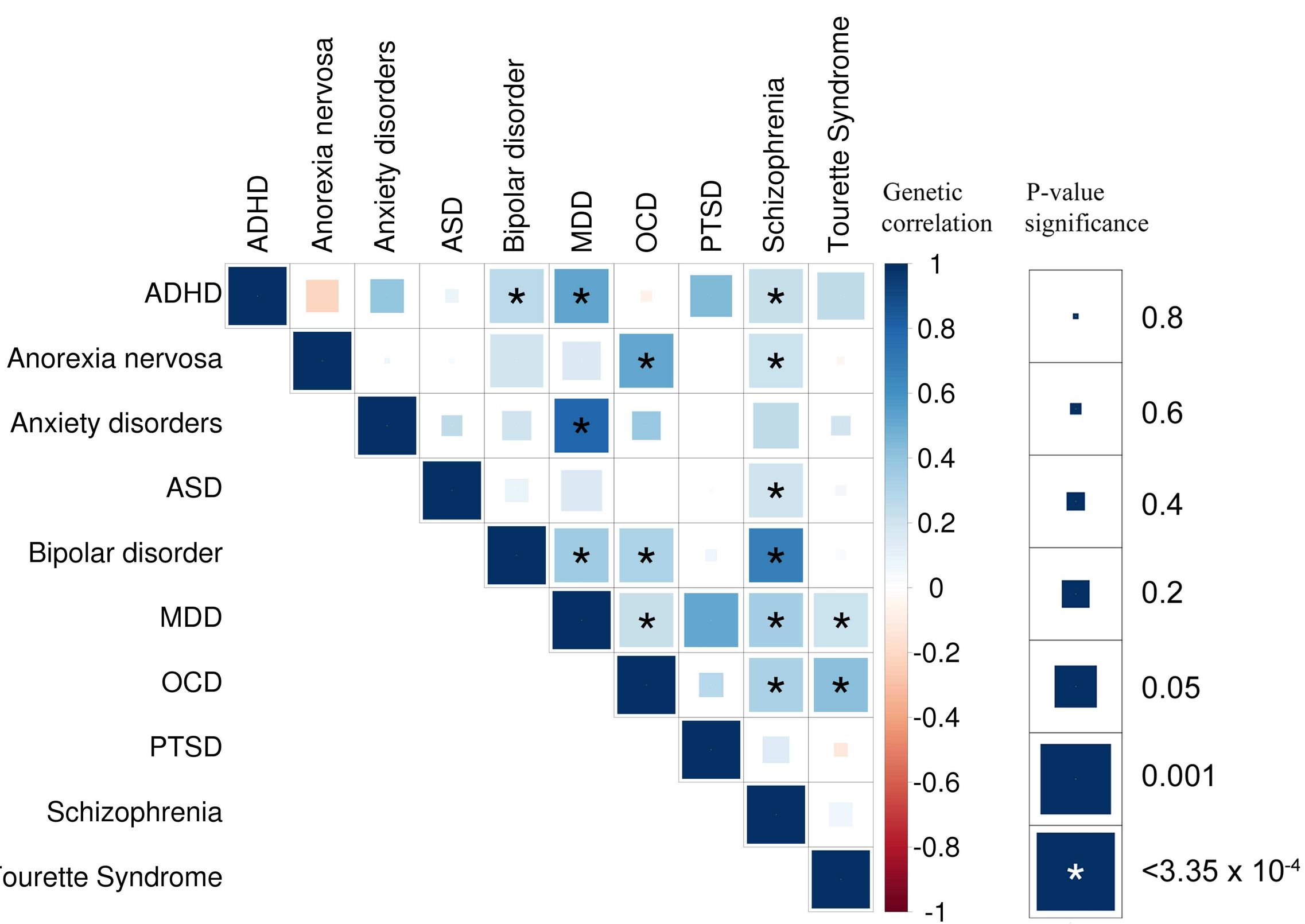
http://www.thessgac.org/data
http://www.thessgac.org/data
http://www.tweelingenregister.org/GPC/
http://ctg.cncr.nl/software/summary_statistics
http://www.thessgac.org/data
http://www.med.unc.edu/pgc/results-and-downloads

---

https://www.broadinstitute.org/collaboration/giant
https://www.broadinstitute.org/collaboration/giant
http://www.ibdgenetics.org/downloads.html
http://www.cardiogramplusc4d.org/data-downloads/

---

amsportal.ukbiobank.ac.uk


ADHD
Anorexia nervosa
Anxiety disorders
ASD
Bipolar disorder
MDD
OCD
PTSD
Schizophrenia
Tourette Syndrome
Genetic correlation
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
-1
P-value significance
0.8
0.6
0.4
0.2
0.05
0.001
<3.35 x 10-4

Alzheimer's disease
Epilepsy
Focal epilepsy
Generalized epilepsy
ICH
Ischemic stroke
Early-onset stroke
Migraine
Migraine with aura
Migraine without aura
Multiple sclerosis
Parkinson's disease

Genetic correlation
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
-1

P-value significance
0.8
0.6
0.4
0.2
0.05
0.001
* <3.35 x 10^{-4}

Alzheimer's disease
Epilepsy
Focal epilepsy
Generalized epilepsy
ICH
Ischemic stroke
Early-onset stroke
Migraine
Migraine with aura
Migraine without aura
Multiple sclerosis
Parkinson's disease

ADHD
Anorexia nervosa
Anxiety disorders
ASD
Bipolar disorder
MDD
OCD
PTSD
Schizophrenia
Tourette Syndrome

Genetic correlation
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
-1

P-value significance
0.8
0.6
0.4
0.2
0.05
0.001
* <3.35 x 10^{-4}

ADHD
Anorexia nervosa
Anxiety disorders
ASD
Bipolar disorder
MDD
OCD
PTSD
Schizophrenia
Tourette Syndrome
Alzheimer's disease
Epilepsy
Focal epilepsy
Generalized epilepsy
ICH
Ischemic stroke
Early-onset stroke
Migraine
Migraine with aura
Migraine without aura
Multiple sclerosis

College attainment
Years of education
Cognitive performance
Intelligence

Neuroticism
Extraversion
Conscientiousness
Openness
Depressive symptoms
Subjective well-being

Never/ever smoked
Cigarettes per day

BMI
Height
Crohn's disease
Myocardial infarction

Genetic correlation
1
0.8
0.6
0.4
0.2
0
-0.2
-0.4
-0.6
-0.8
-1

P-value significance
0.8
0.6
0.4
0.2
0.05
0.001
* <2.30 x 10^{-4}